Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1600RXA

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 4	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 5	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 6	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 7	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 8	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 9	MAR 22	EMBASE is now updated on a daily basis
NEWS 10	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 11	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 12	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 13	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 14	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 15	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS 16	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 17	MAY 11	KOREAPAT updates resume
NEWS 18	MAY 19	Derwent World Patents Index to be reloaded and enhanced

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available after June 2006

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* *

COMPLETE THE STN SURVEY - APRIL 27 THROUGH MAY 31

Dear valued STN customer,

In an effort to enhance your experience with STN, we would like to better understand what you find useful. Please take approximately 5 minutes to complete a web survey.

If you provide us with your name, login ID, and e-mail address, you will be entered in a drawing to win a free iPod(R). Your responses will be kept confidential and will help us make future improvements to STN.

Take survey: http://www.zoomerang.com/survey.zgi?p=WEB2259HNKWTUW

Thank you in advance for your participation.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:47:10 ON 27 MAY 2006

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:47:17 ON 27 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 MAY 2006 HIGHEST RN 885721-85-7
DICTIONARY FILE UPDATES: 26 MAY 2006 HIGHEST RN 885721-85-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

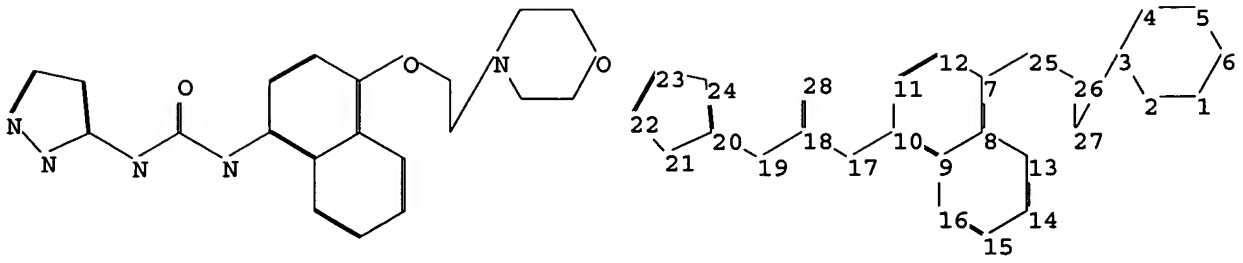
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10727214.str

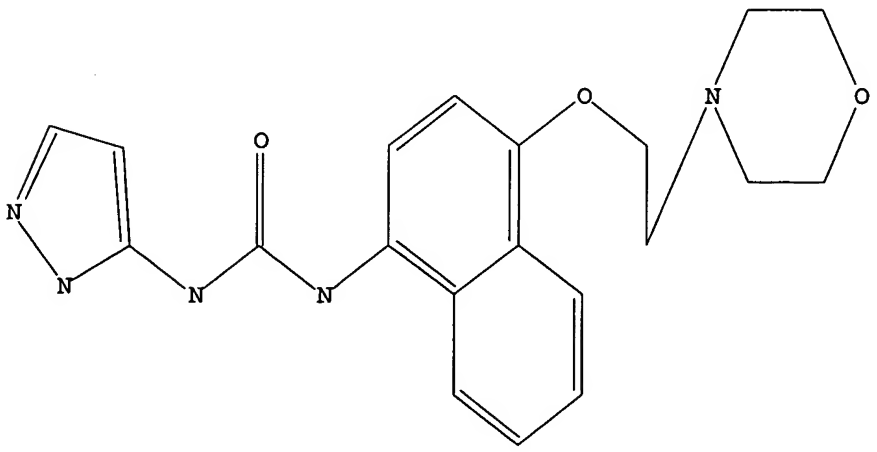


chain nodes :
17 18 19 25 26 27 28
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 20 21 22 23 24
chain bonds :
3-27 7-25 10-17 17-18 18-19 18-28 19-20 25-26 26-27
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-12 7-8 8-9 8-13 9-10 9-16 10-11 11-12 13-14
14-15 15-16 20-21 20-24 21-22 22-23 23-24
exact/norm bonds :
1-2 1-6 2-3 3-4 3-27 4-5 5-6 7-25 10-17 17-18 18-19 18-28 19-20 20-21
20-24 21-22 22-23 23-24 25-26
exact bonds :
26-27
normalized bonds :
7-12 7-8 8-9 8-13 9-10 9-16 10-11 11-12 13-14 14-15 15-16

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 11:47:32 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 10 TO ITERATE

100.0% PROCESSED 10 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11 TO 389
PROJECTED ANSWERS: 8 TO 329

L2 8 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 11:47:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 119 TO ITERATE

100.0% PROCESSED 119 ITERATIONS 98 ANSWERS
SEARCH TIME: 00.00.01

L3 98 SEA SSS FUL L1

=> s l3 and caplus/lc
50676714 CAPLUS/LC
L4 98 L3 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 171.70 171.91

FILE 'CAPLUS' ENTERED AT 11:47:42 ON 27 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 May 2006 VOL 144 ISS 23
FILE LAST UPDATED: 26 May 2006 (20060526/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L5 61 L3

=> s l3 and ethanol
61 L3
247266 ETHANOL

```
          1120 ETHANOLS
        247810 ETHANOL
                 (ETHANOL OR ETHANOLS)
L6           3 L3 AND ETHANOL

=> d ibib abs hitstr 1-3
```

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:149262 CAPLUS
DOCUMENT NUMBER: 144:239931
TITLE: Pharmaceutical compositions for the treatment of respiratory and gastrointestinal disorders
INVENTOR(S): Jung, Birgit; Himmelsbach, Frank
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma Gmbh & Co. KG
SOURCE: PCT Int. Appl., 321 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015775	A2	20060216	WO 2005-EP8385	20050803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006035893	A1	20060216	US 2005-189643	20050726
PRIORITY APPLN. INFO.:			EP 2004-18808 A	20040807

OTHER SOURCE(S): MARPAT 144:239931

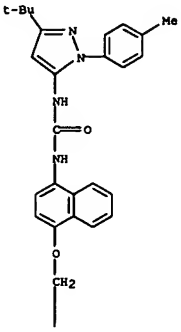
AB The present invention relates to novel pharmaceutical compns. comprising at least 1 EGFR kinase inhibitor and at least one addnl. active compound selected from β-2 mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase inhibitors, NK1 antagonists and endothelin-antagonists, processes for preparing the compns. and the use thereof as drugs in the treatment of respiratory or gastrointestinal complaints, as well as inflammatory diseases of the joints, the skin or the eyes. Thus, an inhalable powder contained an EGFR kinase inhibitor 150, formoterol fumarate dihydrate 50, and lactose 12,300 mg/capsule.

IT **285983-48-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treatment of respiratory and gastrointestinal disorders)

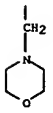
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:546485 CAPLUS
DOCUMENT NUMBER: 141:94322
TITLE: Process for the preparation of a pure polymorph of an N-pyrazolyl-N'-naphthylurea
INVENTOR(S): Samstag, Wendelin; Koch, Gunter
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056783	A1	20040708	WO 2003-EP14128	20031212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004138216	A1	20040715	US 2003-727214	20031203
CA 2511325	AA	20040708	CA 2003-2511325	20031212
AU 2003298178	A1	20040714	AU 2003-298178	20031212
EP 1581502	A1	20051005	EP 2003-795888	20031212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006513185	T2	20060420	JP 2004-561284	20031212
PRIORITY APPLN. INFO.:			US 2002-436136P P	20021223
			WO 2003-EP14128 W	20031212

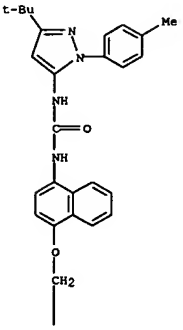
AB The invention relates to an improved process for the preparation of a polymorph of 1-(tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl]urea (I) by crystallization from an alc., wherein the improvement is that crude I is treated with **ethanol**. The preparation of I and its polymorph are given.

IT **285983-48-4P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of polymorph of pyrazolylnaphthylurea)

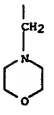
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:942809 CAPLUS
DOCUMENT NUMBER: 138:24709
TITLE: Preparation of pyrazole compounds and bis pyrazole-1H-pyrazole intermediates as antiinflammatory agents
INVENTOR(S): Kapadia, Suresh R.; Song, Jinhua J.; Yee, Nathan K.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. 6,372,773. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6492529	B1	20021210	US 2002-67492	20020205
US 6319921	B1	20011120	US 2000-484638	20000118
US 6333325	B1	20011225	US 2001-871559	20010531
US 6329415	B1	20011211	US 2001-891579	20010626
US 2002065285	A1	20020530	US 2001-891820	20010626
US 6506748	B2	20030114		
US 6372773	B1	20020416	US 2001-920899	20010802

PRIORITY APPLN. INFO.: US 2000-484638 A3 20000118
US 2001-920899 A2 20010802
US 1999-116400P P 19990119
US 2001-891579 A3 20010626

OTHER SOURCE(S): CASREACT 138:24709; MARPAT 138:24709
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

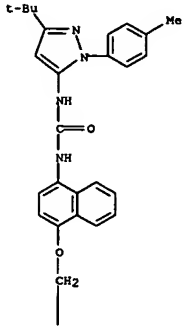
AB Pyrazole compds., e.g. I, as well as bis pyrazole-1H-pyrazole intermediate compds. e.g. II, were prepared The compds. are useful in pharmaceutic compns. for treating diseases or pathol. conditions involving inflammation such as chronic inflammatory diseases. All prepared compds. had IC50 < 10 mM for inhibition of TNFα in lipopolysaccharide stimulated THP cells.

IT **285983-44-0P 285983-47-3P 285983-48-4P 285983-49-5P 285983-51-9P 285983-54-2P 285983-56-4P 285983-57-5P 285983-58-6P 285983-64-4P 285983-68-8P 285983-87-1P 285983-89-3P 285983-90-6P 477844-69-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazole compds. and bis pyrazole-1H-pyrazole intermediates as antiinflammatory agents)

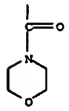
L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 285983-44-0 CAPLUS
CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



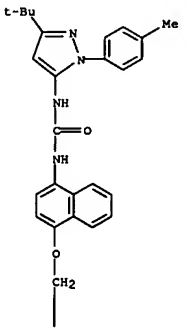
PAGE 2-A



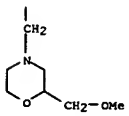
RN 285983-47-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(methoxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



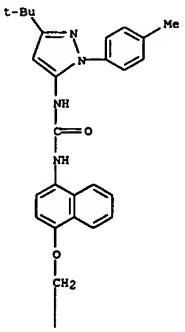
PAGE 2-A



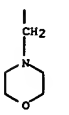
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



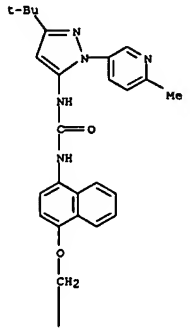
PAGE 2-A



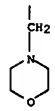
RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



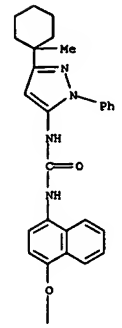
PAGE 2-A



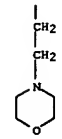
RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



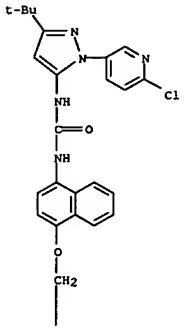
PAGE 2-A



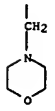
RN 285983-54-2 CAPLUS
CN Urea, N-[1-(6-chloro-3-pyridinyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



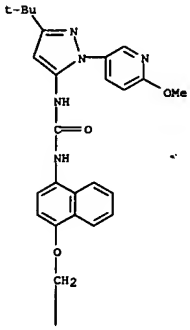
PAGE 2-A



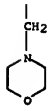
RN 285983-56-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



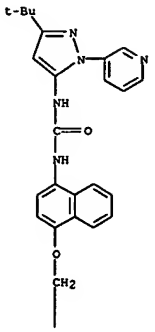
PAGE 2-A



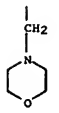
RN 285983-57-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



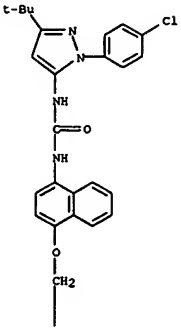
PAGE 2-A



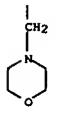
RN 285983-58-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



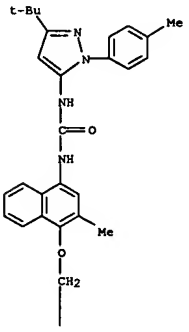
PAGE 2-A



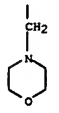
RN 285983-64-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[3-methyl-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



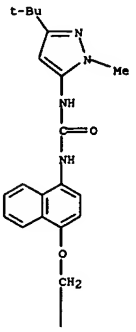
PAGE 2-A



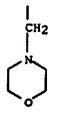
RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

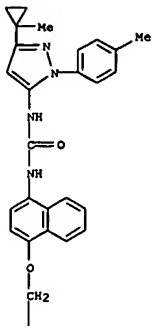


PAGE 2-A

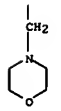


RN 285983-87-1 CAPLUS
CN Urea,
N-[3-(1-methylcyclopropyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

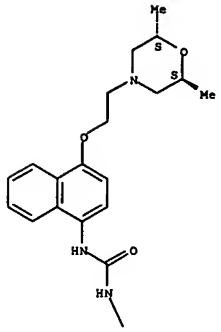


RN 285983-89-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

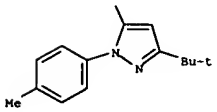
Relative stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

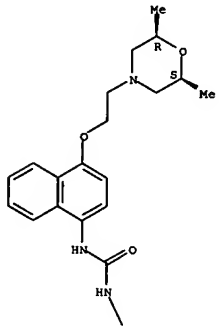


RN 285983-90-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

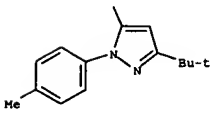
Relative stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



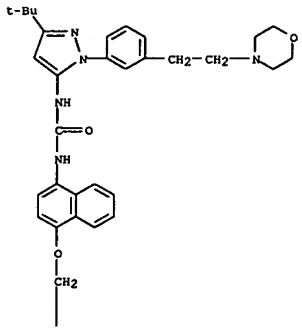
PAGE 2-A



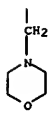
RN 477844-69-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[3-[2-(4-morpholinyl)ethyl]phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

```
=> s l5 not l6
L7          58 L5 NOT L6

=> d ibib abs hitstr 1-58
```

L7 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:191897 CAPLUS
DOCUMENT NUMBER: 144:280573
TITLE: Controlled and directed local delivery of anti-inflammatory compositions
INVENTOR(S): McKay, William F.; Zanella, John M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 932,878.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006046961	A1	20060302	US 2005-91348	20050328
US 2006046960	A1	20060302	US 2004-932878	20040902
WO 2006028939	A1	20060316	WO 2005-US31234	20050901

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-932878 A2 20040902
US 2005-91348 A 20050328

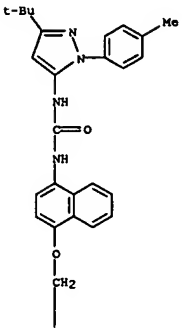
AB The invention provides a method for alleviating pain associated with neuromuscular or skeletal injury or inflammation by controlled and directed delivery of 1 or more biol. response modifiers to inhibit the inflammatory response which ultimately causes acute or chronic pain. Controlled and directed delivery can be provided by implantable or infusion pumps, implantable controlled release devices, or by sustained release compns. comprising biol. response modifiers. PLGA and bone morphogenetic protein were dissolved in methylene chloride and water, resp., to give microspheres.

IT **285983-48-4**, BIRB 796
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled and directed local delivery of anti-inflammatory compns.)

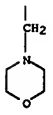
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:165118 CAPLUS
DOCUMENT NUMBER: 144:246354
TITLE: Signal transduction therapy with rationally designed kinase inhibitors
AUTHOR(S): Keri, Gyorgy; Orfi, Laszlo; Eros, Daniel; Hegymegi-Barakonyi, Balint; Szantai-Kis, Csaba; Horvath, Zoltan; Waczek, Frigyes; Marosfalvi, Jeno; Szabadkai, Istvan; Pato, Janos; Greff, Zoltan; Hafenbradl, Doris; Daub, Henrik; Muller, Gerhard; Klebl, Bert; Ullrich, Axel
CORPORATE SOURCE: Vichem Chemie Research Ltd., Budapest, H-1022, Hung.
SOURCE: Current Signal Transduction Therapy (2006), 1(1), 67-95
CODEN: CSTTBV; ISSN: 1574-3624
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

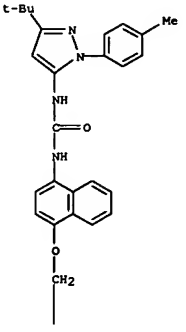
AB A review. Signal transduction therapy has become one of the most important areas of drug research. Signaling disorders represent a major cause for the pathol. states and many of the recently identified validated target mols. of drug research are signal transduction related macromols., mostly kinases. Rational drug design is aimed to achieve the selective inhibition of distinct pathol. relevant signaling enzymes or receptors. In the previous years, the concept of rational drug design has been expanded for a complex process including pathomechanism-based target selection, target validation, structural biol., mol. modeling, structure-activity relationships, pharmacophore-based compound selection and pharmacol. optimization. The two main branches of the chemical rational drug design are structure-based design and ligand-based design. Some important examples for the application of 3D structure-based rational drug design in the development of clin. relevant kinase inhibitors are presented. The Nested Chemical Library (NCL) technol. is a ligand-based design approach and relies on a knowledge-based approach, where focused libraries around published leads and selected cores are used to generate extended pharmacophore models (Prediction Oriented QSAR). NCL was designed on the platform of a diverse kinase inhibitor library, consisting of small mol. heterocycles, which are organized around 108 core structures. Some examples for testing the library on various targets and Prediction Oriented QSAR models will also be presented. The core elements of the kinase family-biased masterkey concept are the so-called privileged structures that emerge from a sophisticated mol. design and optimization process that encodes for a target family-wide structural commonality in ligand binding. The combination of a kinase family-wide imprinted commonality with addnl. structural fragments in the mol. periphery of a once established privileged structure allows to synthesize highly active and selective kinase inhibitors. In addition, several kinase inhibitors in preclin. or clin. development and application of 3D structure based rational drug design in the development of clin. relevant kinase inhibitors are reviewed.

IT **285983-48-4**, BIRB-796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(signal transduction therapy with rationally designed kinase inhibitors)

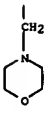
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 224 THERE ARE 224 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:156543 CAPLUS
DOCUMENT NUMBER: 144:343065
TITLE: NMR characterization of kinase p38 dynamics in free and ligand-bound forms
AUTHOR(S): Vogtherr, Martin; Saxena, Krishna; Hoelder, Swen; Grimme, Susanne; Betz, Marco; Schieborr, Ulrich; Pescatore, Barbara; Robin, Michel; Delarbre, Laure; Langer, Thomas; Wendt, K. Ulrich; Schwalbe, Harald
CORPORATE SOURCE: Institute for Organic Chemistry and Chemical Biology Center for Biomolecular Magnetic Resonance, Johann Wolfgang Goethe-University Frankfurt, Frankfurt am Main, 60439, Germany
SOURCE: Angewandte Chemie, International Edition (2006), 45(6), 993-997
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

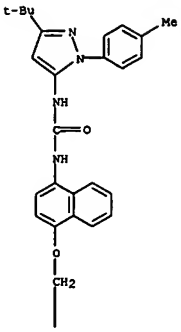
AB In its apo state kinase p38 effects slow motions that can be detected in the NMR spectrum. One of the affected parts is the pharmacol. interesting DFG motif. Diarylurea inhibitors that bind to the DFG-out conformation lock this motif in a defined state, whereas DFG-in inhibitors that bind to the adjacent hinge region leave the flexibility of the DFG motif unaffected as seen in crystal structure of the complex of p38 with the inhibitor SB203580.

IT **285983-48-4**, Birb796
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(NMR characterization of kinase p38 dynamics in free and ligand-bound forms)

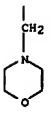
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1328591 CAPLUS
DOCUMENT NUMBER: 144:57567
TITLE: Autonomous replication promoter for stem cells
INVENTOR(S): Hirao, Atushi; Ito, Keisuke; Suda, Toshio; Sakurada, Kazuhiro
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; Keio University
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121320	A1	20051222	WO 2005-JP10642	20050610

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-172057 A 20040610

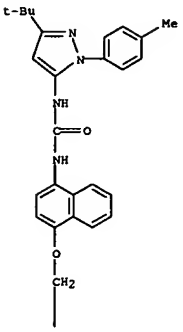
AB It is intended to provide an autonomous replication promoter for stem cells; a preventive for cancer; a preventive or a remedy for diseases accompanied by tissue disruption or tissue failure; a medium for culturing stem cells obtained by adding the above-described autonomous replication promoter for stem cells; a stem cell cultured in this medium; a method of producing stem cells; or a method of screening an autonomous replication promoter for hematopoietic stem cells. Namely, an autonomous replication promoter for stem cells which contains, as the active ingredient, a substance having at least one activity selected from among an activity of inhibiting the production of active oxygen in stem cells, an activity of eliminating produced active oxygen to thereby lessen active oxygen in stem cells, and an activity of inhibiting an intracellular signaling system induced by the active oxygen; a preventive for cancer; a preventive or a remedy for diseases accompanied by tissue disruption or tissue failure; a medium for culturing stem cells obtained by adding the above-described autonomous replication promoter for stem cells; a stem cell cultured in this medium; a method of producing stem cells; or a method of screening an autonomous replication promoter for hematopoietic stem cells.

IT **285983-48-4**, BIRB796BS
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(autonomous replication promoter for stem cells)

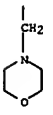
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

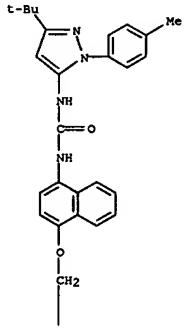


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

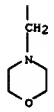
ACCESSION NUMBER: 2005:1072941 CAPLUS
DOCUMENT NUMBER: 143:359650
TITLE: Reply to BIRB-796 is not an effective ABL(T315I) inhibitor
AUTHOR(S): Fabian, Miles A.; Biggs, William H.; Treiber, Daniel K.; Zarrinkar, Patrick P.; Lockhart, David J.
CORPORATE SOURCE: Ambit Biosciences, San Diego, CA, 92121, USA
SOURCE: Nature Biotechnology (2005), 23(10), 1210-1211
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A polemic in response to T. O'Hare and B. Drucker (ibid., 1209).
IT **285983-48-4**, BIRB-796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BIRB-796 is not an effective ABL(T315I) inhibitor)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



L7 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



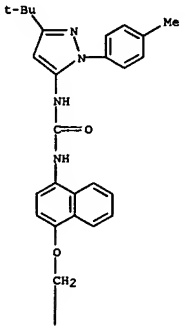
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 6 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

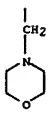
ACCESSION NUMBER: 2005:1072940 CAPLUS
DOCUMENT NUMBER: 143:359649
TITLE: BIRB-796 is not an effective ABL(T315I) inhibitor
AUTHOR(S): O'Hare, Thomas; Druker, Brian J.
CORPORATE SOURCE: Howard Hughes Medical Institute, Oregon Health & Science University Cancer Institute, Portland, OR, 97239, USA
SOURCE: Nature Biotechnology (2005), 23(10), 1209-1210
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A polemic in response to Fabian et al. (ibid., 23, 329-336, 2005).
IT **285983-48-4**, BIRB-796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BIRB-796 is not an effective ABL(T315I) inhibitor)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



L7 ANSWER 6 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

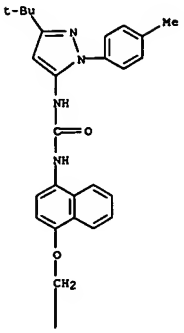
ACCESSION NUMBER: 2005:1011557 CAPLUS
DOCUMENT NUMBER: 143:379100
TITLE: High Affinity Targets of Protein Kinase Inhibitors Have Similar Residues at the Positions Energetically Important for Binding
AUTHOR(S): Sheinerman, Felix B.; Giraud, Elie; Laoui, Abdelazize
CORPORATE SOURCE: Sanofi Aventis Group 1041, Informatics, Aventis, Bridgewater, NJ, 08807, USA
SOURCE: Journal of Molecular Biology (2005), 352(5), 1134-1156
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibition of protein kinase activity is a focus of intense drug discovery efforts in several therapeutic areas. Major challenges facing the field include understanding of the factors determining the selectivity of kinase inhibitors and the development of compds. with the desired selectivity profile. Here, we report the anal. of sequence variability among high and low affinity targets of eight different small mol. kinase inhibitors (BIRB796, Tarceva, NU6102, Gleevec, SB203580, balanol, H89, PP1). It is observed that all high affinity targets of each inhibitor are found among a relatively small number of kinases, which have similar residues at the specific positions important for binding. The findings are highly statistically significant, and allow one to exclude the majority of kinases in a genome from a list of likely targets for an inhibitor. The findings have implications for the design of novel inhibitors with a desired selectivity profile (e.g. targeted at multiple kinases), the discovery of new targets for kinase inhibitor drugs, comparative anal. of different in vivo models, and the design of "a-la-carte" chemical libraries tailored for individual kinases.

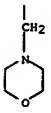
IT **285983-48-4**, BIRB796
RL: PAC (Pharmacological activity); BIOL (Biological study)
(high affinity targets of protein kinase inhibitors have similar residues at positions energetically important for binding)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004352 CAPLUS
DOCUMENT NUMBER: 143:279459
TITLE: Compositions and methods for preventing and treating skin and hair conditions
INVENTOR(S): David, Nathaniel E.
PATENT ASSIGNEE(S): VVII NewCo 2003, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203111	A1	20050915	US 2004-799867	20040312
WO 2005091891	A2	20051006	WO 2005-US6300	20050225

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

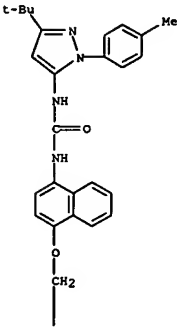
PRIORITY APPLN. INFO.: US 2004-799540 A 20040311
US 2004-799867 A 20040312
US 2004-810391 A 20040326

AB The present invention discloses compns. and methods for the prevention and treatment of skin and hair diseases, such as, for example, alopecia, psoriasis, and keloids. In one embodiment, the present invention discloses a method for preventing and treating hair loss by applying locally to a region lacking hair a p38α MAP kinase inhibitor. The p38α MAP kinase inhibitor is preferably formulated as a gel, ointment, spray or solution that can be applied topically, transdermally, or s.c. to the targeted region. The p38 inhibitor is especially RDP-58, AMG-548, BIRB-796, CNI-1493, VX-702 or VX-745.

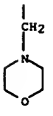
IT **285983-48-4**, BIRB-796
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor; p38α MAP kinase inhibitor for preventing and treating skin and hair conditions)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

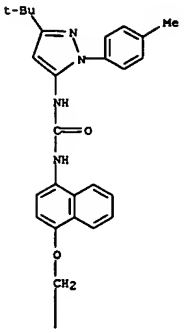
ACCESSION NUMBER: 2005:781086 CAPLUS
DOCUMENT NUMBER: 143:222029
TITLE: Inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases
AUTHOR(S): Carter, Todd A.; Wodicka, Lisa M.; Shah, Neil P.; Velasco, Anne Marie; Fabian, Miles A.; Treiber, Daniel K.; Milanov, Zdravko V.; Atteridge, Corey E.; Biggs, William H., III; Edeen, Philip T.; Floyd, Mark; Ford, Julia M.; Grotzfeld, Robert M.; Herrgard, Sanna; Insko, Darren E.; Mehta, Shamal A.; Patel, Hitesh K.; Pao, William; Sawyers, Charles L.; Varmus, Harold; Zarrinkar, Patrick P.; Lockhart, David J.
CORPORATE SOURCE: Ambit, Inc., San Diego, CA, 92121, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2005), 102(31), 11011-11016
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To realize the full potential of targeted protein kinase inhibitors for the treatment of cancer, it is important to address the emergence of drug resistance in treated patients. Mutant forms of BCR-ABL, KIT, and the EGF receptor (EGFR) have been found that confer resistance to the drugs imatinib, gefitinib, and erlotinib. The mutations weaken or prevent drug binding, and interestingly, one of the most common sites of mutation in all three kinases is a highly conserved "gatekeeper" threonine residue near the kinase active site. We have identified existing clin. compds. that bind and inhibit drug-resistant mutant variants of ABL, KIT, and EGFR. We found that the Aurora kinase inhibitor VX-680 and the p38 inhibitor BIRB-796 inhibit the imatinib- and BMS-354825-resistant ABL(T315I) kinase. The KIT/FLT3 inhibitor SU-11248 potently inhibits the imatinib-resistant KIT(V559D/T670I) kinase, consistent with the clin. efficacy of SU-11248 against imatinib-resistant gastrointestinal tumors, and the EGFR inhibitors EKB-569 and Cl-1033, but not GW-572016 and ZD-6474, potently inhibit the gefitinib- and erlotinib-resistant EGFR(L858R/T790M) kinase. EKB-569 and Cl-1033 are already in clin. trials, and our results suggest that they should be considered for testing in the treatment of gefitinib/erlotinib-resistant non-small cell lung cancer. The results highlight the strategy of screening existing clin. compds. against newly identified drug-resistant mutant variants to find compds. that may serve as starting points for the development of next-generation drugs, or that could be used directly to treat patients that have acquired resistance to first-generation targeted therapy.

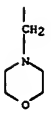
IT **285983-48-4**, BIRB-796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases for screening of antitumor agents)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

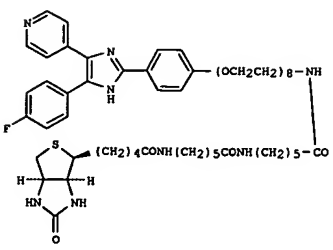
ACCESSION NUMBER: 2005:614536 CAPLUS
DOCUMENT NUMBER: 143:115392
TITLE: Preparation of conjugated small molecules for diagnostic and therapeutic use
INVENTOR(S): Grotzfeld, Robert M.; Milanov, Zdravko V.; Patel, Hitesh K.; Lai, Andiliy G.; Mehta, Shamal A.; Lockhart, David J.
PATENT ASSIGNEE(S): Ambit Biosciences Corp., USA
SOURCE: U.S. Pat. Appl. Publ., 63 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005153371	A1	20050714	US 2005-31638	20050107
WO 2005067644	A2	20050728	WO 2005-US456	20050107
WO 2005067644	A3	20051013		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-535173P P 20040107
US 2004-557941P P 20040330

GI



I

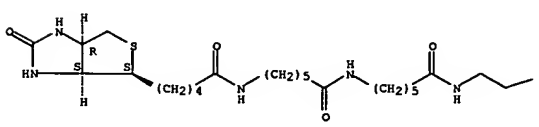
L7 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

AB Provided herein are linker compds. and conjugates that include the linker compds. In one embodiment, the linker compds. comprise 2 or 3 residues of 6-aminohexanoic acid and optionally 7-10 residues of polyethyleneglycol (PEG). The linker compds. are useful in forming conjugates with one or more components useful in biopharmaceutical or bioanal. applications. In particular, the biopharmaceutically useful compds. are kinase inhibitors. The conjugates described herein have utility in a variety of diagnostic, separation, and therapeutic applications. Thus, I was prepared from SB 202190, PEG-azide and the biotin-linker compound

IT **857891-99-7P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of conjugated biotins for diagnostic and therapeutic use)
RN 857891-99-7 CAPLUS
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[45-[4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-2-morpholinyl]-6,13-dioxo-17,20,23,26,29,32,35,38,41-nonaoxa-7,14,44-triazapentatetracont-1-yl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)

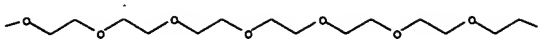
Absolute stereochemistry.

PAGE 1-A

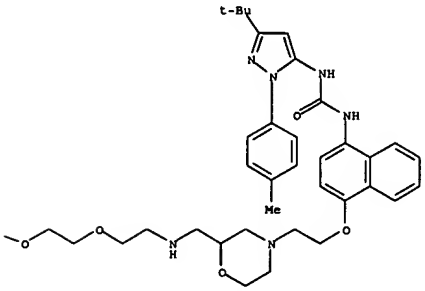


L7 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-B

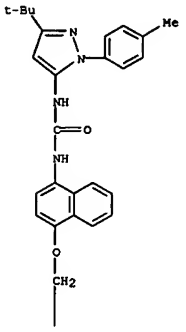


PAGE 1-C

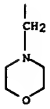


L7 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



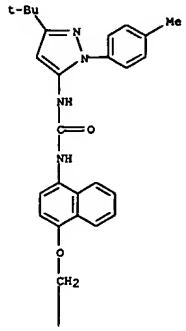
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:610501 CAPLUS
DOCUMENT NUMBER: 143:243882
TITLE: Time-resolved Forster resonance energy transfer assays for the binding of nucleotide and protein substrates to protein kinase
AUTHOR(S): Zhang, Wen Xiao; Wang, Ruixiu; Wisniewski, Douglas; Marcy, Alice I.; LoGrasso, Philip; Lisnock, Jean-Marie; Cummings, Richard T.; Thompson, James E.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Analytical Biochemistry (2005), 343(1), 76-83
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have developed assays for the binding of nucleotide and protein substrates to p38α protein kinase based on time-resolved Forster resonance energy transfer. P38α was biotinylated by addition of a sequence that targets biotin to a single lysine when coexpressed with biotin ligase in Escherichia coli, allowing formation of a complex between a streptavidin "LANCE" europium chelate conjugate and p38α. When this reagent was combined with M39AF, a p38 inhibitor containing a fluorescent moiety whose excitation wavelengths match the emission wavelengths of the europium chelate, a change in ratio of light emitted at 665 nm/615 nm is detected. Less than 100 pM complex was detected with a signal/background ratio of >30-fold. The complex exhibits slow, tight binding kinetics where the apparent Kd decreases with a relaxation time of 21 min at 125 pM biotin-p38α. Preincubating inhibitors or ATP with biotin-p38α and adding M39AF as a competitor yielded IC50s consistent with those measured by enzyme assay for the activated form of biotin-p38α. The same technique was also used to measure affinity of inhibitors for the unphosphorylated and catalytically inactive form of biotin-p38α. To measure affinity of p38α for its protein substrate MK2, the authors incubated biotin-p38α with a glutathione S-transferase MK2 fusion protein. Detection of the complex after incubation with streptavidin-allophycocyanin and a LANCE-conjugated anti-GST allowed measurement of affinity of MK2 for biotin-p38α and detection of 0.5 nM p38α · MK2 complex with signal/background ratio >5-fold. Competition with unbiotinylated p38α yielded an IC50 value of 5 nM. Activation of either p38α or MK2 had no effect on the measured Kd. M39AF was found to bind in a ternary complex with p38α·MK2 with lower affinity than that observed in the binary complex with p38α alone.
IT 285983-48-4, BIRB-796
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand; time-resolved Forster resonance energy transfer assays for binding of nucleotide and protein substrates to p38α protein kinase)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

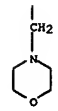
L7 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:594355 CAPLUS
DOCUMENT NUMBER: 144:80285
TITLE: p38 MAP kinase inhibitors: Many are made, but few are chosen
AUTHOR(S): Dominguez, Celia; Powers, David A.; Tamayo, Nuria
CORPORATE SOURCE: Chemistry Research & Discovery Medicinal Chemistry, Amgen Inc, Thousand Oaks, CA, 91320-179, USA
SOURCE: Current Opinion in Drug Discovery & Development (2005), 8(4), 421-430
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The mitogen-activated protein kinase (MAPK) p38 is a Ser/Thr kinase, originally isolated from lipopolysaccharide-stimulated monocytes. There are 4 isoforms of the enzyme (p38α, p38β, p38γ and p38δ), which differ in tissue distribution, regulation of kinase activation, and subsequent phosphorylation of downstream substrates. These enzymes also differ in sensitivity to p38 MAPK inhibitors. The most thoroughly studied isoform is p38α, for which activation was observed in many hematopoietic and non-hematopoietic cell types upon appropriate stimuli. P38α kinase is involved in the biosynthesis of the cytokines tumor necrosis factor-α and interleukin-1β at the translational and transcriptional level. MAPK p38α represents a point of convergence for multiple signaling processes that are activated during inflammation, making it a key potential target for the modulation of cytokine production The discovery and publication of p38α and a pyridinyl-imidazole-based p38α inhibitor initiated a huge effort by many companies to develop p38α inhibitors as potential treatments for inflammatory diseases. Herein, a brief overview is provided of the discovery and development of AMG-548 (Amgen Inc), a selective and efficacious p38α inhibitor, and its pharmacodynamic effects in a 1st-in-human study. Data from a phase I multidose clin. trial are also included. In addition, other p38α inhibitors that have advanced to clin. trials over the last 3 years are discussed, such as BIRB-796 (Boehringer Ingelheim Pharmaceuticals Inc). SCIO-469 and SCIO-323 (Scios Inc), and VX-702 (Vertex Pharmaceuticals Inc/Kissei Pharmaceutical Co).
IT 285983-48-4, BIRB-796
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p38 MAP kinase inhibitors)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:547258 CAPLUS
DOCUMENT NUMBER: 143:65486
TITLE: Polymorphs of BIRB 796 and their preparation
INVENTOR(S): Smoliga, John A.; Vitous, Jana
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005137195	A1	20050623	US 2004-10975	20041213
WO 2005063715	A1	20050714	WO 2004-US41627	20041213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-530834P P 20031218

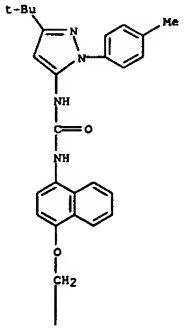
AB Disclosed are polymorphs of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea and processes from making the same. A polymorph form VI of BIRB 796 possessing a solid-solid polymorphic transformation in the range of 138 -145° to Form VII which subsequently melts in the range of 177-186°. A process of preparing a BIRB 796 polymorph form VI process comprises: dissolving BIRB 796 in a solvent chosen from Et acetate, Bu acetate, iso-Bu acetate, iso-Pr acetate, Pr acetate and tert-Bu acetate at reflux temperature; cooling the solution to about room temperature and subsequently collecting the crystallizing solid. XRPD data of polymorph form VI of BIRB 796 are listed.

IT 285983-48-4, BIRB 796
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polymorphs of BIRB 796 and their preparation)

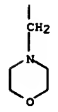
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:490261 CAPLUS
DOCUMENT NUMBER: 143:19989
TITLE: Methods and compositions for the treatment of immunoinflammatory disorders using pyrazolopyridine compounds in combination with corticosteroids or other agents
INVENTOR(S): Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Smith, Brendan; Slavonic, Michael S.; Auspitz, Benjamin A.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

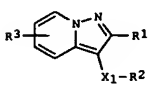
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051293	A2	20050609	WO 2004-US38512	20041117
WO 2005051293	A3	20060302		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005187203	A1	20050825	US 2004-992878	20041119

PRIORITY APPLN. INFO.: US 2003-524117P P 20031121

OTHER SOURCE(S): MARPAT 143:19989
GI



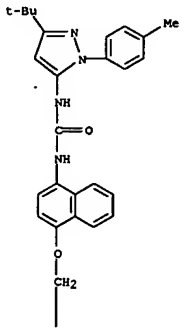
I

AB The invention features a method for treating an immunoinflammatory disorder by administering I (R1, R2 = H, C1-7 alkyl, C2-7 alkenyl C2-7 alkynyl, C2-6 heterocyclyl, etc.; R3 = H, halo, alkoxy, C1-4 alkyl; X1 = C=O, C=N-NH-R4, etc.; R4 = H, acyl), e.g., ibudilast or KC-764, alone or in combination with a corticosteroid, tetra-substituted pyrimidopyrimidine, or other compound The invention also features pharmaceutical compns. including the combination above for the treatment or prevention of an immunoinflammatory disorder. The combination of ibudilast and prednisolone reduced proinflammatory IL-1 and TNFα secretion by white blood cells stimulated by PMA-ionomycin in vitro.

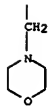
IT 285983-48-4, Doramapimod

L7 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compn. further comprising; treatment of immunoinflammatory disorders using pyrazolopyridine compds. in combination with corticosteroids or other agents)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L7 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:470256 CAPLUS
DOCUMENT NUMBER: 143:20052
TITLE: Urea derivatives as kinase modulators
INVENTOR(S): Milanov, Zdravko V.; Patel, Hitesh K.; Grotzfeld, Robert M.; Mehta, Shamal A.; Andiliy, Lai G.; Lockhart, David J.
PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA
SOURCE: PCT Int. Appl., 350 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

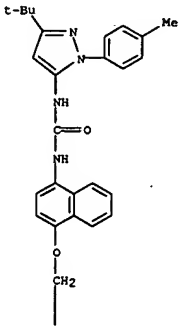
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048948	A2	20050602	WO 2004-US38288	20041115
WO 2005048948	A3	20050728		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148605	A1	20050707	US 2004-989745	20041115
US 2005165031	A1	20050728	US 2004-989814	20041115
US 2005165024	A1	20050728	US 2004-989824	20041115
US 2005165074	A1	20050728	US 2004-990007	20041115
US 2005171171	A1	20050804	US 2004-989766	20041115
US 2005171172	A1	20050804	US 2004-989823	20041115
US 2005192314	A1	20050901	US 2004-990195	20041115
US 2005197371	A1	20050908	US 2004-990194	20041115
US 2005261315	A1	20051124	US 2004-989623	20041115
US 2005267182	A1	20051201	US 2004-989717	20041115

PRIORITY APPLN. INFO.: US 2003-520273P P 20031113
US 2003-527094P P 20031203
US 2003-531082P P 20031218
US 2003-531243P P 20031218

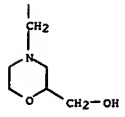
OTHER SOURCE(S): MARPAT 143:20052
AB The invention provides methods and compns. for treating conditions mediated by various kinases wherein derivs. of urea compds. are employed. The invention also provides methods of using the compds. and/or compns. in the treatment of a variety of diseases and unwanted conditions in subjects such as cellular proliferative disorders.
IT 852671-64-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urea derivs. as kinase modulators for treatment of cellular proliferative disorders)

L7 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 852671-64-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(hydroxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



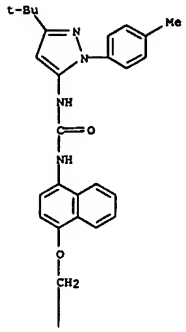
PAGE 2-A



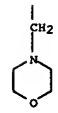
L7 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:418520 CAPLUS
DOCUMENT NUMBER: 143:111403
TITLE: BIRB796 Inhibits All p38 MAPK Isoforms in Vitro and in Vivo
AUTHOR(S): Kuma, Yvonne; Sabio, Guadalupe; Bain, Jenny; Shpiro, Natalia; Marquez, Rodolfo; Cuenda, Ana
CORPORATE SOURCE: Medical Research Council Protein Phosphorylation Unit, University of Dundee, Dundee, DD1 5EH, UK
SOURCE: Journal of Biological Chemistry (2005), 280(20), 19472-19479
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The compound BIRB796 inhibits the stress-activated protein kinases p38α and p38β and is undergoing clin. trials for the treatment of inflammatory diseases. Here we report that BIRB796 also inhibits the activity and the activation of SAPK3/p38γ. This occurs at higher concns. of BIRB796 than those that inhibit p38α and p38β and at lower concns. than those that inhibit the activation of JNK isoforms. We also show that at these concns., BIRB796 blocks the stress-induced phosphorylation of the scaffold protein SAP97, further establishing that this is a physiol. substrate of SAPK3/p38γ. Our results demonstrate that BIRB796, in combination with SB203580, a compound that inhibits p38α and p38β, but not the other p38 isoforms, can be used to identify physiol. substrates of SAPK3/p38γ as well as those of p38α and p38β.
IT 285983-48-4, BIRB796
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BIRB796 inhibits all p38 MAPK isoforms in vitro and in vivo)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:394529 CAPLUS
DOCUMENT NUMBER: 142:451800
TITLE: Techniques to treat neurological disorders by attenuating the production of proinflammatory mediators
INVENTOR(S): Shafer, Lisa L.
PATENT ASSIGNEE(S): Medtronic, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005095246	A1	20050505	US 2004-972157	20041022
WO 2005039393	A2	20050506	WO 2004-US35194	20041022
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006013802	A1	20060119	US 2005-152944	20050615

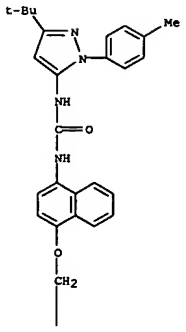
PRIORITY APPLN. INFO.:

US 2003-514137P	P	20031024
US 2004-972157	A2	20041022
US 2004-972177	A2	20041022
US 2004-638633P	P	20041222

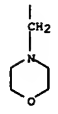
AB Methods and devices to attenuate tumor necrosis factor (TNF) and other pro-inflammatory mediators in the CNS to treat neurol., neurodegenerative, neuropsychiatric disorders, pain and brain injury are described. More particularly, TNF-blocking agents that target intracellular signals and downstream effects associated with the production and secretion of TNF are described. Devices described include therapy delivery devices comprising a reservoir capable of housing a TNF-blocking agent and a catheter operably coupled to the device and adapted to deliver the TNF-blocking agent to a target site within a subject.
IT 285983-48-4, BIRB 796
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery systems for blockers of proinflammatory mediators for treatment of neurol. disorders)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:369225 CAPLUS
DOCUMENT NUMBER: 142:404248
TITLE: Tetrasubstituted pyrimidopyrimidines, alone or in combination with other agents, for the treatment of immunoinflammatory disorders
INVENTOR(S): Keith, Curtis; Borisy, Alexis; Zimmermann, Grant R.; Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Hurst, Nicole; Foley, Michael A.; Slavonic, Michael S.; Smith, Brendan; Auspitz, Benjamin A.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037203	A2	20050428	WO 2004-US33656	20041013
WO 2005037203	A3	20060316		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119160	A1	20050602	US 2004-966228	20041015

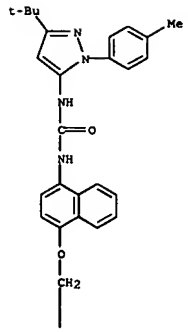
PRIORITY APPLN. INFO.:

US 2003-512415P	P	20031015

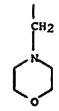
AB The invention discloses a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering to the patient a tetrasubstituted pyrimidopyrimidine, either alone or in combination with one or more addnl. agents. The invention also features a composition containing a tetra-substituted pyrimidopyrimidine in combination with one or more addnl. agents.
IT 285983-48-4, Doramapimod
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidopyrimidine tetrasubstituted derivs., alone or in combination with other agents, for treatment of immunoinflammatory disorders)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:301463 CAPLUS
DOCUMENT NUMBER: 143:3640
TITLE: HierS: Hierarchical Scaffold Clustering Using Topological Chemical Graphs
AUTHOR(S): Wilkens, Steven J.; Janes, Jeff; Su, Andrew I.
CORPORATE SOURCE: Genomics Institute of the Novartis Research Foundation, San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(9), 3182-3193
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

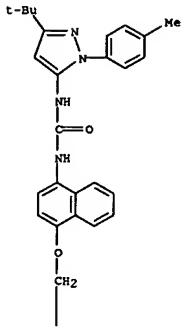
AB An exhaustive ring-based algorithm, HierS, has been developed in order to provide an intuitive approach to compound clustering for analyzing high-throughput screening results. The recursive algorithm rapidly identifies all possible ring-delimited substructures within a set of compds. Mols. are grouped by shared ring substructures (scaffolds) so that common scaffolds obtain higher membership. Once all of the scaffolds for a set of compds. are identified, the hierarchical structural relationships between the scaffold structures are established. The complex network of hierarchical relationships is then utilized to navigate compds. in a structurally directed fashion. When the scaffold hierarchy is traversed, over-represented structural features can be rapidly identified so that excess compds. that contain them can be removed without significantly impacting the structural diversity landscape of the compound set. Furthermore, the removed compds. can provide the opportunity to follow-up on active compds. that had previously been discarded because of practical limitations on follow-up capacity. A Web-based interface has been developed that incorporates this algorithm in order to allow for an interactive anal. In addition, biol. data are coupled to scaffolds by the inclusion of activity histograms, which indicate how the compds. in each scaffold class performed in previous high-throughput screening campaigns.

IT 285983-48-4, BIRB 796
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(HierS algorithm for high-throughput screening of inhibitors)

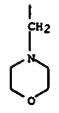
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:250817 CAPLUS
DOCUMENT NUMBER: 143:90243
TITLE: Classifying "kinase inhibitor-likeness" by using machine-learning methods
AUTHOR(S): Briem, Hans; Guenther, Judith
CORPORATE SOURCE: Research Center Europe CDCC/Computational Chemistry, Schering AG, Berlin, 13342, Germany
SOURCE: ChemBioChem (2005), 6(3), 558-566
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By using an inhouse data set of small-mol. structures, encoded by Ghose-Crippen parameters, several machine learning techniques were applied to distinguish between kinase inhibitors and other mols. with no reported activity on any protein kinase. All 4 approaches pursued-support-vector machines (SVM), artificial neural networks (ANN), k nearest neighbor classification with GA-optimized feature selection (GA/kNN), and recursive partitioning (RP)-proved capable of providing a reasonable discrimination. Nevertheless, substantial differences in performance among the methods were observed For all techniques tested, the use of a consensus vote of the 13 different models derived improved the quality of the predictions in terms of accuracy, precision, recall, and F1 value. Support-vector machines, followed by the GA/kNN combination, outperformed the other techniques when comparing the average of individual models. By using the resp. majority votes, the prediction of neural networks yielded the highest F1 value, followed by SVMs.

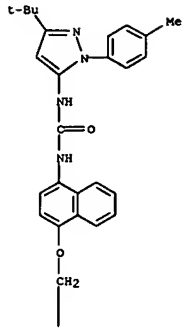
IT 285983-48-4, BIRB796
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(classifying kinase inhibitor-likeness by machine-learning methods)

RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

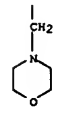
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:238947 CAPLUS
DOCUMENT NUMBER: 142:316831
TITLE: Preparation of amides of pyrazolamines and anilines as
well as analogs as cytokine inhibitors for the treatment of inflammatory diseases
INVENTOR(S): Boman, Erik; Ceide, Susana C.; Dahl, Russell; Delaet, Nancy G. J.; Ernst, Justin; Montalban, Antonio G.; Kahl, Jeffrey D.; Larson, Christopher; Miller, Stephen; Nakanishi, Hiroshi; Roberts, Edward; Saiah, Eddine; Sullivan, Robert; Wang, Zhijun
PATENT ASSIGNEE(S): Kemia, Inc., USA
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

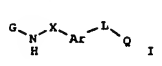
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023761	A2	20050317	WO 2004-US29372	20040910
WO 2005023761	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2538820	AA	20050317	CA 2004-2538820	20040910
US 2005107399	A1	20050519	US 2004-939324	20040910

PRIORITY APPLN. INFO.:

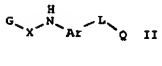
US 2003-502569P	P	20030911
US 2003-531234P	P	20031218
US 2004-575704P	P	20040528
US 2004-585012P	P	20040702
WO 2004-US29372	W	20040910

OTHER SOURCE(S): MARPAT 142:316831
GI

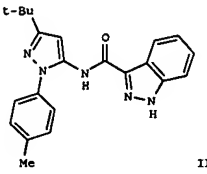
L7 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I



II



III

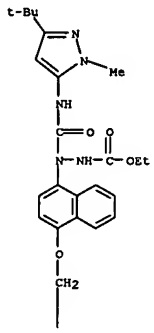
AB Title compds., such as I and II (four Markush structures are claimed), wherein X = C(O), C(S) or CH2; G = (un)substituted carbocyclyl or heterocyclyl; Ar = indazolyl, indolyl, pyrazolyl, alkyl, etc.; L = covalent bond or (un)substituted carbon chain; Q = H, (un)substituted amino, cycloalkyl, heterocyclyl, alkoxy or sulfonyl; with some limitations and exclusions, and stereoisomers, tautomers, solvates, prodrugs and pharmaceutically acceptable salts thereof, were prepared as cytokine inhibitors. For instance, cyclization of p-tolylhydrazine hydrochloride with 4,4-dimethyl-3-oxopentanenitrile to the corresponding pyrazolamine (92% yield) followed by EDC-mediated coupling with indazole-3-carboxylic acid gave indazolopyrazole III (40% yield). I were found to have activity in the TNFa ELISA assay, with some compds. having IC50 < 10 μM. Therefore, I and their pharmaceutical compns. are useful in preventing or treating conditions mediated by cytokines, such as arthritis and inflammatory diseases.

IT 848148-66-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of amides of pyrazolamines and anilines as well as analogs as cytokine inhibitors)

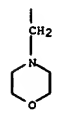
RN 848148-66-3 CAPLUS
CN Hydrazinecarboxylic acid, 2-[[[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]amino]carbonyl]-2-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-, ethyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:219452 CAPLUS
DOCUMENT NUMBER: 142:441281
TITLE: A small molecule-kinase interaction map for clinical kinase inhibitors
AUTHOR(S): Fabian, Miles A.; Biggs, William H.; Treiber, Daniel K.; Atteridge, Corey E.; Azimioara, Mihai D.; Benedetti, Michael G.; Carter, Todd A.; Ciceri, Pietro; Edeen, Philip T.; Floyd, Mark; Ford, Julia M.; Galvin, Margaret; Gerlach, Jay L.; Grotzfeld, Robert M.; Herrgard, Sanna; Insko, Darren E.; Insko, Michael A.; Lai, Andiliy G.; Lelias, Jean-Michel; Mehta, Shamal A.; Milanov, Zdravko V.; Velasco, Anne Marie; Wodicka, Lisa M.; Patel, Hitesh K.; Zarrinkar, Patrick P.; Lockhart, David J.
CORPORATE SOURCE: Ambit Biosciences, San Diego, CA, 92121, USA
SOURCE: Nature Biotechnology (2005), 23(3), 329-336
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

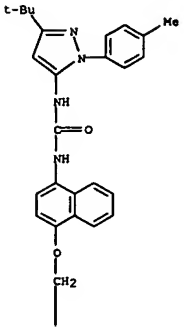
AB Kinase inhibitors show great promise as a new class of therapeutics. Here the authors describe an efficient way to determine kinase inhibitor specificity by measuring binding of small mols. to the ATP site of kinases. The authors have profiled 20 kinase inhibitors, including 16 that are approved drugs or in clin. development, against a panel of 119 protein kinases. The authors find that specificity varies widely and is not strongly correlated with chemical structure or the identity of the intended target. Many novel interactions were identified, including tight binding of the p38 inhibitor BIRB-796 to an imatinib-resistant variant of the ABL kinase, and binding of imatinib to the SRC-family kinase LCK. The authors also show that mutations in the epidermal growth factor receptor (EGFR) found in gefitinib-responsive patients do not affect the binding affinity of gefitinib or erlotinib. Our results represent a systematic small mol.-protein interaction map for clin. compds. across a large number of related proteins.

IT **285983-48-4**, BIRB-796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol.-kinase interaction map for clin. kinase inhibitors)

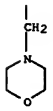
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:177881 CAPLUS
DOCUMENT NUMBER: 142:274025
TITLE: Methods using a combination of a p38 MAP kinase inhibitor with another active agent for the treatment of chronic obstructive pulmonary disease (COPD) and pulmonary hypertension
INVENTOR(S): Gupta, Abhya; Iacono, Philippe Didier; Kelash-Cannavo, Linda Jean; Madwed, Jeffrey B.; Park, Jung-Yong; Way, Susan Lynn; Yazdanian, Mehran
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim Pharma GmbH & Co. KG; Boehringer Ingelheim France S.A.S.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018624	A2	20050303	WO 2004-US27013	20040819
WO 2005018624	A3	20050506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266719	A1	20050303	AU 2004-266719	20040819
CA 2536293	AA	20050303	CA 2004-2536293	20040819
US 2005148555	A1	20050707	US 2004-921448	20040819
EP 1658060	A2	20060524	EP 2004-781654	20040819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-497376P P 20030822
WO 2004-US27013 W 20040819

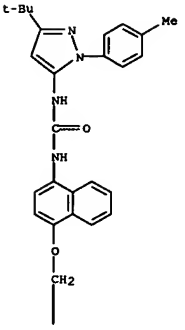
AB Methods are disclosed for treating COPD and pulmonary hypertension using p38 MAP Kinase inhibitors in combination with one or more other active ingredients.

IT **285983-48-4 847024-06-0 847024-07-1 847024-08-2 847024-09-3 847024-10-6 847024-11-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p38 MAP kinase inhibitor combination with another active agent for treatment of chronic obstructive pulmonary disease and pulmonary hypertension)

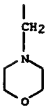
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

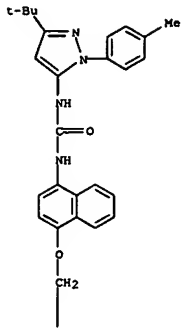


RN 847024-06-0 CAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-, cis-, mixt. with N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (9CI) (CA INDEX NAME)

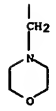
CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

PAGE 1-A



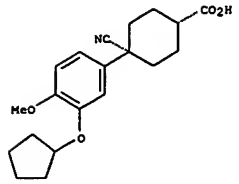
PAGE 2-A



CM 2

CRN 153259-65-5
CMF C20 H25 N O4

Relative stereochemistry.

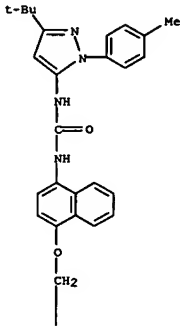


RN 847024-07-1 CAPLUS
CN Benzamide, 3-(cyclopropylmethoxy)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-, mixt. with N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (9CI) (CA INDEX NAME)

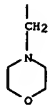
CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

PAGE 1-A

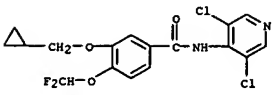


PAGE 2-A



CM 2

CRN 162401-32-3
CMF C17 H14 Cl2 F2 N2 O3

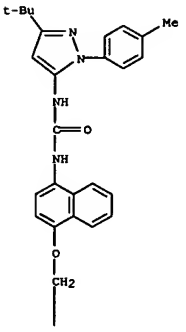


RN 847024-08-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-, mixt. with 4-hydroxy-α1-[[[6-(4-phenylbutoxy)hexyl]amino]methyl]-1,3-benzenedimethanol (9CI) (CA INDEX NAME)

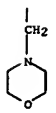
CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

PAGE 1-A

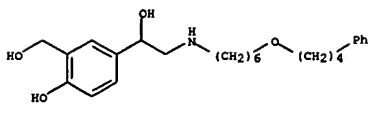


PAGE 2-A



CM 2

CRN 89365-50-4
CMF C25 H37 N O4



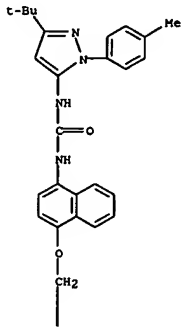
RN 847024-09-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-

[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-, mixt. with rel-N-[2-hydroxy-5-[(1R)-1-hydroxy-2-[[(1R)-2-(4-methoxyphenyl)-1-methylethyl]amino]ethyl]phenyl]formamide (9CI) (CA INDEX NAME)

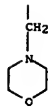
CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

PAGE 1-A



PAGE 2-A

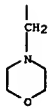


CM 2

CRN 73573-87-2
CMF C19 H24 N2 O4

Relative stereochemistry.

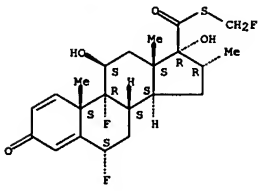
PAGE 2-A



CM 2

CRN 90566-53-3
CMF C22 H27 F3 O4 S

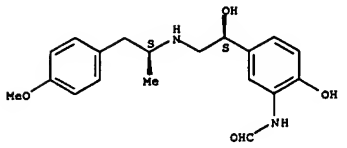
Absolute stereochemistry.



RN 847024-11-7 CAPLUS
CN Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11β,16α)-, mixt. with N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (9CI) (CA INDEX NAME)

CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

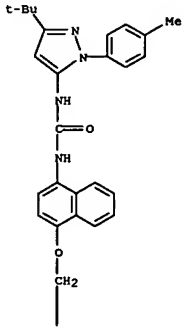


RN 847024-10-6 CAPLUS
CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11,17-dihydroxy-16-methyl-3-oxo-, S-(fluoromethyl) ester, (6α,11β,16α,17.alpha.)-, mixt. with N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (9CI) (CA INDEX NAME)

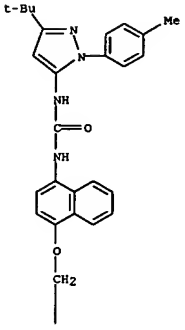
CM 1

CRN 285983-48-4
CMF C31 H37 N5 O3

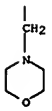
PAGE 1-A



PAGE 1-A



PAGE 2-A

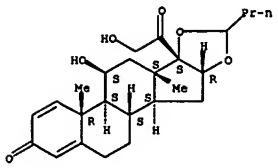


CM 2

CRN 51333-22-3
CMF C25 H34 O6

Absolute stereochemistry.

L7 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L7 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:99319 CAPLUS
DOCUMENT NUMBER: 142:172181
TITLE: Novel targets of protein kinase-inhibiting drugs for novel disease therapies
INVENTOR(S): Biggs, William H., III; Carter, Todd; Fabian, Miles A.; Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiber, Daniel Kelly; Edeen, Phillip
PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009367	A2	20050203	WO 2004-US23325	20040719
WO 2005009367	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-488513P P 20030717

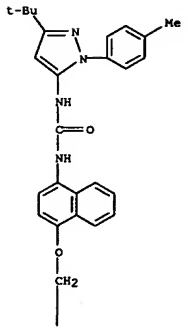
AB The invention is directed to the identification and use of addnl. targets of BIRB 796, imatinib mesylate, and BAY 43-9006. The new targets of BIRB 796, imatinib mesylate, and BAY 43-9006 can be used to screen for suitable therapeutic compds. Also, novel therapeutic and prophylactic uses for BIRB 796, imatinib mesylate, and BAY 43-9006 are disclosed herein. Protein targets of the drugs were identified using a phage-based competition assay using a panel of 69 proteins including 48 kinases.

IT **285983-48-4**, BIRB 796
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel targets of protein kinase-inhibiting drugs for novel disease therapies)

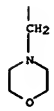
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:89214 CAPLUS
DOCUMENT NUMBER: 142:332348
TITLE: Prospective Exploration of Synthetically Feasible, Medicinally Relevant Chemical Space
AUTHOR(S): Schuerer, Stephan C.; Tyagi, Prashant; Muskal, Steven M.
CORPORATE SOURCE: Sertanty, Inc., San Diego, CA, 92121, USA
SOURCE: Journal of Chemical Information and Modeling (2005), 45(2), 239-248
CODEN: JCISD8; ISSN: 1549-9596
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

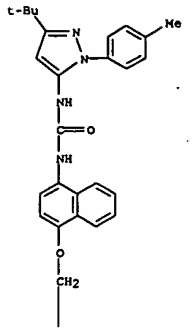
AB We describe a novel approach to direct the exploration of chemical space in an effort to balance synthetic accessibility and medicinal relevancy prior to exptl. work. Reaction transforms containing empirical reactivity and compatibility information are dynamically assembled into reaction sequences (vProtocols) utilizing com. available starting material feedstock. These vProtocols are evolved and optimized by a genetic algorithm, which leverages fitness functions based on predicted properties of generated mol. products. We present the underlying concepts, methodol. and initial results of this prospective approach.

IT **285983-48-4**, BIRB 796
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(prospective exploration of synthetically feasible, medicinally relevant chemical space)

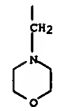
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1156620 CAPLUS
DOCUMENT NUMBER: 142:71185
TITLE: Phage display assay for detecting protein binding by screening libraries of compounds against phage-displayed polypeptides
INVENTOR(S): Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiver, Daniel Kelly
PATENT ASSIGNEE(S): Ambit Biosciences, Inc., USA; Ambit Biosciences Corporation
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113556	A2	20041229	WO 2004-US19943	20040621
WO 2004113556	C1	20050310		
WO 2004113556	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004250256	A1	20041229	AU 2004-250256	20040621
CA 2526847	AA	20041229	CA 2004-2526847	20040621
US 2005009099	A1	20050113	US 2004-873835	20040621
EP 1644513	A2	20060412	EP 2004-776903	20040621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-480587P	P 20030620
			WO 2004-US19943	W 20040621

AB The present invention provides methods and kits for identifying interactions between test mols. and polypeptides. Preferably the polypeptides are displayed on phage and the interactions are evaluated in the presence of reference moieties that are optionally attached to a solid support. One aspect of the invention is a method for determining the binding affinities of a test mol. to different polypeptides from a set of polypeptides. In another aspect, the invention provides a method of screening libraries of compds. against one or more polypeptides. The present invention also provides methods of quantifying the interaction between phage-displayed polypeptides and test mols. Kits for performing the assays described herein are also provided. The invention is based on the ability to assess the affinity of the interaction, if any, of a test mol. and a phage-displayed polypeptide in the presence of a reference moiety that binds the displayed polypeptide. The test mol. may be considered as

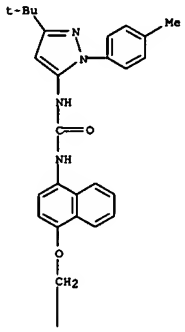
L7 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

a competitor against the ref. moiety for binding to the displayed polypeptide. Therefore, in one aspect, the invention is directed to a method to apply phage display technol., wherein the method comprises simultaneously contacting a phage-displayed polypeptide with a ref. moiety immobilized on a solid support and a test mol. at a sufficient concn. to decrease the binding of the displayed polypeptide to the ref. moiety. The concns. of the test mol. necessary to diminish binding of the displayed polypeptide from the ref. moiety may be used to det. a dissocn. const. (Kd) for the test mol. Human kinases expressed as fusions to T7 bacteriophage particles and a small set of immobilized ligands that bind to the ATP site of one or more kinases were used. Six compds. were tested for the ability to compete with the interaction between p38 and immobilized SB202190: SB202190 (without biotin modification); SB203580 (a pyridinylimidazole closely related to SB202190) (Table 1); SB202474 (a pyridinylimidazole that does not bindp 38); BIRB-796 (Table 1); VX-745 (Table 1); and purvalanol A (a CDK2 inhibitor). Competition with unmodified SB202190, SB203580, BIRB-796 and VX-745 decreased by 1000-fold or more the amt. of phage-displayed p38 bound to the solid support, whereas neither SB202474 nor purvalanol A had a significant effect (Fig. 1B). These results demonstrate that the binding assay correctly discriminates between compds. that bind to the kinase, and those that do not, and yields accurate binding consts.

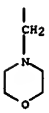
IT **285983-48-4**, BIRB-796
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reference kinase modulator, decreased the amount of phage-displayed p38 bound to the solid support; phage display assay for detecting protein binding by screening libraries of compds. against phage-displayed polypeptides)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

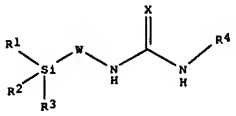
ACCESSION NUMBER: 2004:1154725 CAPLUS
DOCUMENT NUMBER: 142:74722
TITLE: Silylated heterocyclylurea derivatives as cytokine-inhibitors
INVENTOR(S): Miller, David John; Montana, John Gary; Showell, Graham Andrew; Warneck, Julie Belinda Hazel
PATENT ASSIGNEE(S): Amedis Pharmaceuticals Ltd., UK
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113352	A1	20041229	WO 2004-GB2562	20040616

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	GB 2003-14292	A 20030619
	GB 2003-28149	A 20031204
	GB 2004-1244	A 20040120

OTHER SOURCE(S): CASREACT 142:74722; MARPAT 142:74722
GI



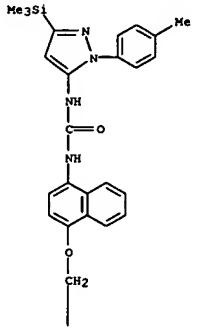
I

AB The preparation of title compds. I (R1, R2, R3 = same or different and are each alkyl, alkyl-aryl, alkyl-cycloalkyl; R1-Si-R2 taken together form heterocycloalkyl; R4 = aryl, heteroaryl, either of which is optionally substituted with Y-R5; R5 = alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl; W = heterocyclylene optionally substituted with alkyl, alkyl-aryl, alkyl-cycloalkyl, aryl, heteroaryl, alkyl-heteroaryl, alkyl-heterocycloalkyl; X = O, S; Y = bond, NH, O, S, Si(R6)(R7), alkylene, alkenylene, O-alkyl, S-alkyl, NH-alkyl, Si(R6)(R7)-alkyl; R6, R7 = same or different and are each alkyl; with the proviso that Si(R1)(R2)(R3) is bound to a ring carbon atom of W; or a pharmaceutically acceptable salt thereof, or a prodrug form that is oxidizable or hydrolyzable to form a compd. as defined above), useful as cytokine-inhibitors (no data), is described. Thus, reaction of N-(4-tolyl)-3-trimethylsilylpyrazole-5-carboxylic acid (prepn. given) with diphenylphosphoryl azide followed by treatment with 1-amino-4-(2-morpholin-4-ylethoxy)naphthalene dihydrochloride gave title compd., 1-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]-3-(2-p-tolyl-5-trimethylsilyl-2H-pyrazol-3-yl)urea.

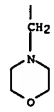
IT **813449-48-8P 813449-51-3P 813449-55-7P**
813449-57-9P 813449-58-0P 813449-59-1P
813449-60-4P 813449-61-5P 813449-62-6P
813449-63-7P 813449-66-0P 813449-67-1P
813449-70-6P 813449-71-7P 813449-73-9P
813449-74-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of silylated heterocyclylurea derivs. as cytokine-inhibitors)

RN 813449-48-8 CAPLUS
CN Urea, N-[1-(4-methylphenyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

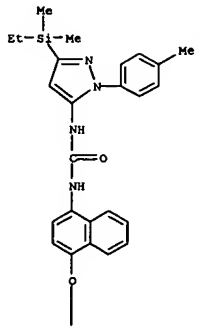


PAGE 2-A

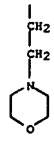


RN 813449-51-3 CAPLUS
CN Urea, N-[3-(ethyldimethylsilyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

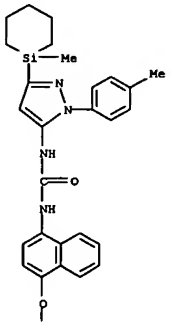


PAGE 2-A

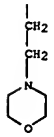


RN 813449-55-7 CAPLUS
CN Urea, N-[1-(4-methylphenyl)-3-(1-methylsilacyclohex-1-yl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

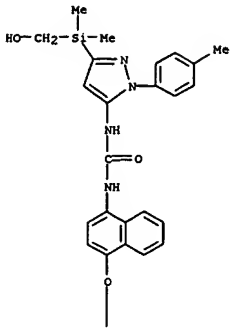


PAGE 2-A

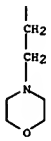


RN 813449-57-9 CAPLUS
CN Urea, N-[3-[(hydroxymethyl)dimethylsilyl]-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

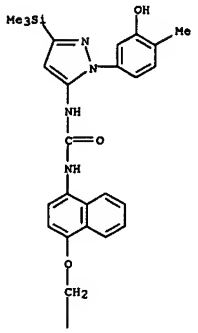


PAGE 2-A

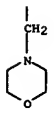


RN 813449-58-0 CAPLUS
CN Urea,
N-[1-(3-hydroxy-4-methylphenyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-
N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



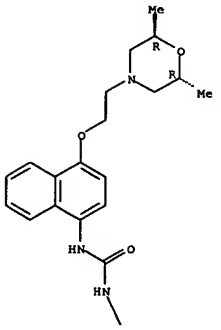
PAGE 2-A



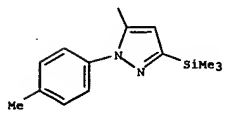
RN 813449-59-1 CAPLUS
CN Urea,
N-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-
N'-[1-(4-methylphenyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-, rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

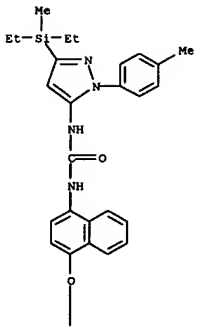


PAGE 2-A

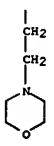


RN 813449-60-4 CAPLUS
CN Urea,
N-[3-(diethylmethylsilyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-
[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

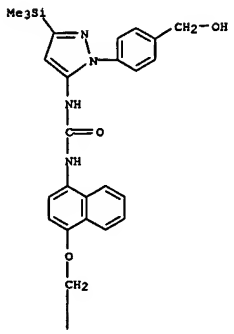


PAGE 2-A

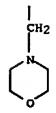


RN 813449-61-5 CAPLUS
CN Urea, N-[1-[4-(hydroxymethyl)phenyl]-3-(trimethylsilyl)-1H-pyrazol-5-yl]-
N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

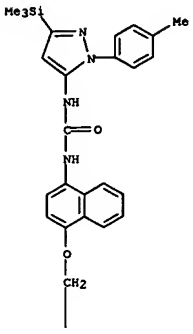


PAGE 2-A

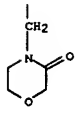


RN 813449-62-6 CAPLUS
CN Urea, N-[1-(4-methylphenyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(3-oxo-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



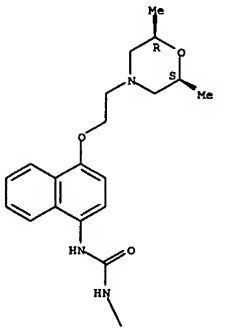
PAGE 2-A



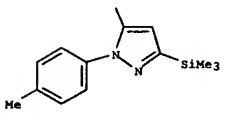
RN 813449-63-7 CAPLUS
CN Urea, N-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-N'-[1-(4-methylphenyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

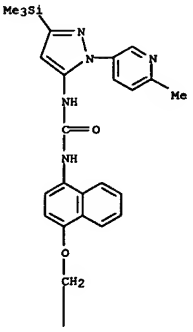


PAGE 2-A

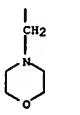


RN 813449-66-0 CAPLUS
CN Urea, N-[1-(6-methyl-3-pyridinyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

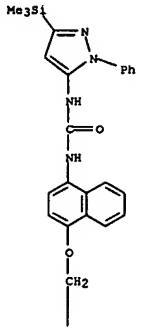


PAGE 2-A

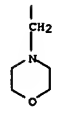


RN 813449-67-1 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-[1-phenyl-3-(trimethylsilyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

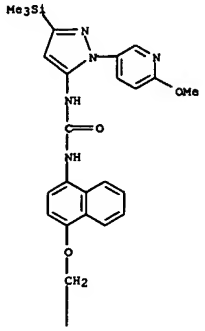


PAGE 2-A

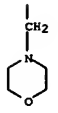


RN 813449-70-6 CAPLUS
CN Urea, N-[1-(6-methoxy-3-pyridinyl)-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

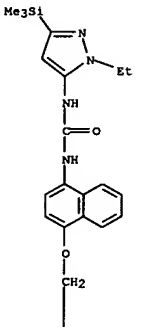


PAGE 2-A

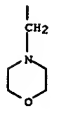


RN 813449-71-7 CAPLUS
CN Urea, N-[1-ethyl-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

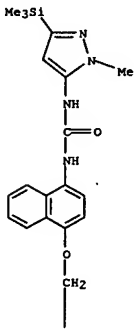


PAGE 2-A

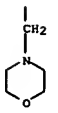


RN 813449-73-9 CAPLUS
CN Urea, N-[1-methyl-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



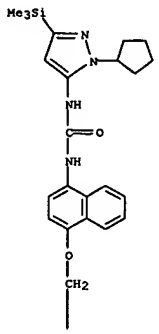
PAGE 2-A



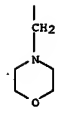
RN 813449-74-0 CAPLUS
CN Urea, N-[1-cyclopentyl-3-(trimethylsilyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1072170 CAPLUS
DOCUMENT NUMBER: 142:190226
TITLE: Interaction Profiles of Protein Kinase-Inhibitor Complexes and Their Application to Virtual Screening
AUTHOR(S): Chuaqui, Claudio; Deng, Zhan; Singh, Juswinder
CORPORATE SOURCE: Computational Drug Design Group, Department of Research Informatics, Biogen Idec, Inc., Cambridge, MA, 01242, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(1), 121-133
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

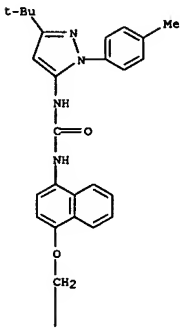
AB A major challenge facing structure-based drug discovery efforts is how to leverage the massive amount of exptl. (x-ray and NMR) and virtual structural information generated from drug discovery projects. Many important drug targets have large nos. of protein-inhibitor complexes, necessitating tools to compare and contrast their similarities and differences. This information would be valuable for understanding potency and selectivity of inhibitors and could be used to define target constraints to assist virtual screening. The authors describe a profile-based approach that enables us to capture the conservation of interactions between a set of protein-ligand receptor complexes. The use of profiles provides a sensitive means to compare multiple inhibitors binding to a drug target. The authors demonstrate the utility of profile-based anal. of small mol. complexes from the protein-kinase family to identify similarities and differences in binding of ATP, p38, and CDK2 compds. to kinases and how these profiles can be applied to differentiate the selectivity of these inhibitors. Importantly, our virtual screening results demonstrate superior enrichment of kinase inhibitors using profile-based methods relative to traditional scoring functions. Interaction-based anal. should provide a valuable tool for understanding inhibitor binding to other important drug targets.

IT **285983-48-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(interaction profiles of protein kinase-inhibitor complexes and their application to virtual screening)

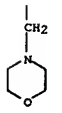
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

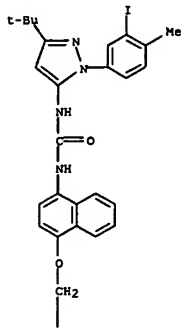
ACCESSION NUMBER: 2004:1040446 CAPLUS
DOCUMENT NUMBER: 142:411280
TITLE: Synthesis of deuterium, tritium, and carbon-14 labeled BIRB 796, a p38 MAP kinase inhibitor
AUTHOR(S): Latli, Bachir
CORPORATE SOURCE: Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Research and Development Center, Ridgefield, CT, 06877, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2004), 47(12), 847-856
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:411280

AB 1-(5-Tert-Butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]urea (BIRB 796), currently in clin. trials for the treatment of inflammatory diseases, is a potent inhibitor of p38 MAP kinase. Labeled BIRB 796 with stable and radioactive isotopes was required for metabolism, distribution, and absorption studies. Carbon-14 labeled BIRB 796 with a specific activity of 2 GBq/mmol (54.2 mCi/mmol) was prepared using [14C]-phosgene under modified Schotten-Baumann conditions; tritium-labeled BIRB 796 with a specific activity of 659 GBq/mmol (17.81 Ci/mmol) was prepared by reductive dehalogenation of iodo-BIRB 796 with tritium gas; and 2H8-BIRB 796 was prepared using morpholine-2,2,3,3,5,5,6,6-2H8 with isotopic enrichment of 98.9 at% 2H.

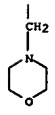
IT **850312-03-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of deuterium, tritium, and carbon-14 labeled BIRB 796, a p38 MAP kinase inhibitor)

RN 850312-03-7 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-iodo-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

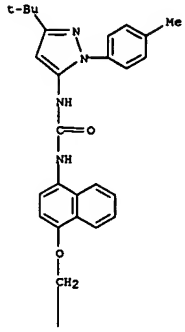


PAGE 2-A

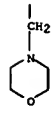


IT **285983-48-4P 850312-08-2P 850312-09-3P**
850312-10-6P 850312-12-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of deuterium, tritium, and carbon-14 labeled BIRB 796, a p38
MAP kinase inhibitor)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

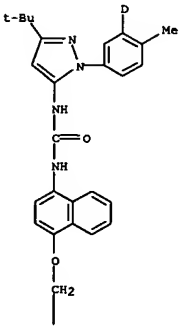


PAGE 2-A

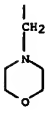


RN 850312-08-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl-3-d)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

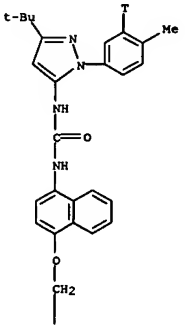


PAGE 2-A

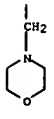


RN 850312-09-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl-3-t)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

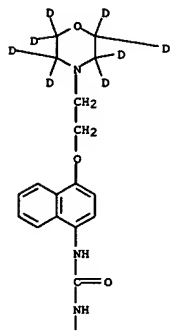


PAGE 2-A

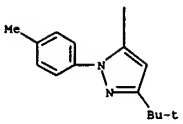


RN 850312-10-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl-2,2,3,3,5,5,6,6-d8)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

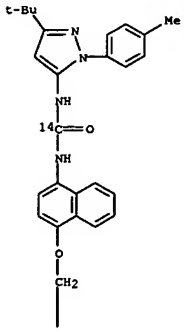


PAGE 2-A

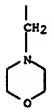


RN 850312-12-8 CAPLUS
CN Urea-14C,
N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-
[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2004:995770 CAPLUS
DOCUMENT NUMBER: 141:406057
TITLE: Methods and reagents for the treatment of diseases and
disorders associated with increased levels of proinflammatory cytokines
INVENTOR(S): Jost-Price, Edward Roydon; Manivasakam, Palaniyandi; Smith, Brendan; Fong, Jason; Auspitz, Benjamin A.; Nichols, M. James; Keith, Curtis; Zimmermann, Grant R.; Brasher, Bradley B.; Sachs, Noah; Chappell, Todd W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 670,488.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229849	A1	20041118	US 2004-777517	20040212
US 2004220153	A1	20041104	US 2003-670488	20030924
US 2005153947	A1	20050714	US 2004-947455	20040920
AU 2004275777	A1	20050407	AU 2004-275777	20040923
CA 2538023	AA	20050407	CA 2004-2538023	20040923
WO 2005030132	A2	20050407	WO 2004-US31195	20040923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005112199	A1	20050526	US 2004-947769	20040923
WO 2005079284	A2	20050901	WO 2005-US4297	20050211
WO 2005079284	A3	20060323		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2002-413040P	P	20020924
US 2002-417261P	P	20021009
US 2002-427424P	P	20021119

US 2002-427526P	P	20021119
US 2003-464753P	P	20030423
US 2003-670488	A2	20030924
US 2003-512415P	P	20031015
US 2003-520446P	P	20031113
US 2004-777517	A1	20040212
US 2004-777518	A	20040212
US 2004-557496P	P	20040330
US 2004-944574	A	20040917
US 2004-947455	A	20040920
WO 2004-US31195	W	20040923

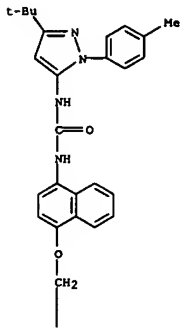
AB The invention features a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering an SSRI or analog or metabolite thereof and, optionally, a corticosteroid or other compound to the patient. The invention also features a pharmaceutical composition containing an SSRI or analog or metabolite thereof and a corticosteroid or other compound for the treatment or prevention of an immunoinflammatory disorder.

IT **285983-48-4**, Doramapimod
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

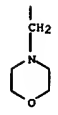
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:839017 CAPLUS
DOCUMENT NUMBER: 142:311699
TITLE: Structural insights into the conformational selectivity of STI-571 and related kinase inhibitors
AUTHOR(S): Mol, Clifford D.; Fabbro, Doriano; Hosfield, David J.
CORPORATE SOURCE: Syrrx Inc, La Jolla, CA, 92121, USA
SOURCE: Current Opinion in Drug Discovery & Development (2004), 7(5), 639-648
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

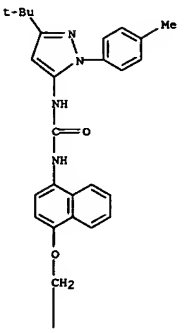
AB A review. STI-571 (Gleevec) is a highly successful cancer drug due to its activity as an inhibitor of the Abelson cytoplasmic tyrosine kinase (Abl), which is constitutively active in a majority of patients with chronic myelogenous leukemia. STI-571 also inhibits two type III receptor tyrosine kinases, c-Kit and platelet-derived growth factor receptor, and functions by targeting inactive conformations of these kinases. This review focuses on recent developments in x-ray co-crystal structure analyses of STI-571 bound to Abl and the c-Kit receptor tyrosine kinase domain, and also three other relevant kinase inhibitor co-crystal structures. The similar structural features of these inactive kinases suggest they will be useful for the successful drug discovery and development of specific and targeted gene-based cancer drugs.

IT 285983-48-4, BIRB-796
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural insights into the conformational selectivity of STI-571 and related kinase inhibitors)

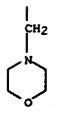
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

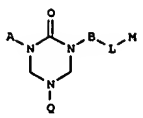
L7 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:756709 CAPLUS
DOCUMENT NUMBER: 141:260780
TITLE: Preparation of 2-oxo-1,3,5-perhydrotriazapine derivatives for treatment of hyper-proliferative, angiogenesis, and inflammatory disorders
INVENTOR(S): Boyer, Stephen; Dumas, Jacques; Phillips, Barton; Scott, William J.; Smith, Roger A.; Chen, Jianqing; James, Benjamin; Wang, Gan
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

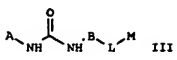
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078746	A2	20040916	WO 2004-US6283	20040301
WO 2004078746	A3	20041202		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2516624	AA	20040916	CA 2004-2516624	20040301
EP 1599466	A2	20051130	EP 2004-716136	20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-450323P P 20030228
WO 2004-US6283 W 20040301

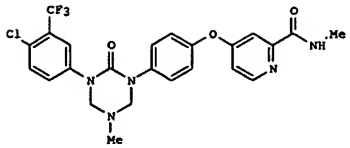
OTHER SOURCE(S): CASREACT 141:260780; MARPAT 141:260780
GI



I



III



II

AB The title compds. I [A, B = 5-10 membered cyclic moieties which optionally substituted with 1-4 substituents selected from the group consisting of R1, OR1, NR1R2, etc.; L = a bridging group selected from -(CH2)m-O-(CH2)n-, -(CH2)m-(CH2)n-, -(CH2)m-C(O)-(CH2)n-, etc.; m, n = 0-4; M = Ph, naphthyl, 5- or 6- membered monocyclic heteroaryl consisting 1-3 heteroatoms selected from O, N, S, etc.; R1, R2 = H, alkyl, Ph, etc.] were prepared for treating hyper-proliferative and angiogenesis disorders.

For example, reaction of 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-2-Pyridinecarboxamide with methylamine hydrochloride and formaldehyde furnished compound II. As prodrugs, compds.

I will release diaryl ureas of the formula III when administrated.

IT **285983-48-4P**

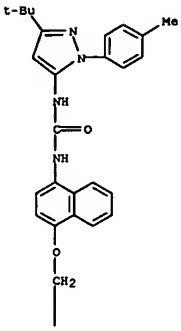
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl 2-oxo-1,3,5-perhydrotriazapine derivs. for treatment of hyper-proliferative, angiogenesis, and inflammatory disorders)

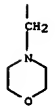
RN 285983-48-4 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



ACCESSION NUMBER: 2004:718295 CAPLUS
DOCUMENT NUMBER: 141:236648
TITLE: Combination therapy for the treatment of immunoinflammatory disorders
INVENTOR(S): Jost-Price, Edward Roydon; Brasher, Bradley B.; Chappel, Todd W.; Manivasakam, Palaniyandi; Sachs, Noah; Smith, Brendan; Auspitz, Benjamin A.
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004073614	A2	20040902	WO 2004-US4077	20040212
WO 2004073614	A3	20041111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004212919	A1	20040902	AU 2004-212919	20040212
CA 2514061	AA	20040902	CA 2004-2514061	20040212
EP 1599212	A2	20051130	EP 2004-710606	20040212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007421	A	20060124	BR 2004-7421	20040212
CN 1761478	A	20060419	CN 2004-80007370	20040212
US 2005192261	A1	20050901	US 2004-940902	20040914
AU 2004273880	A1	20050331	AU 2004-273880	20040915
CA 2537989	AA	20050331	CA 2004-2537989	20040915
WO 2005027839	A2	20050331	WO 2004-US30210	20040915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NO 2005003678	A	20050912	NO 2005-3678	20050729

PRIORITY APPLN. INFO.:

US 2003-447366P	P	20030214
US 2003-447412P	P	20030214
US 2003-447415P	P	20030214
US 2003-447553P	P	20030214
US 2003-447648P	P	20030214
US 2003-464753P	P	20030423
US 2003-503026P	P	20030915
US 2003-447336P	P	20030214
WO 2004-US4077	W	20040212
WO 2004-US30210	W	20040915

AB The invention features a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering a non-steroidal immunophilin-dependent immunosuppressant (NsIDI) and an NsIDI enhancer (NsIDIE) or analog or metabolite thereof to the patient. The invention also features a pharmaceutical composition containing an NsIDI and NsIDIE or analog or metabolite thereof for the treatment or prevention of an immunoinflammatory disorder.

IT **285983-48-4**, Doramapimod

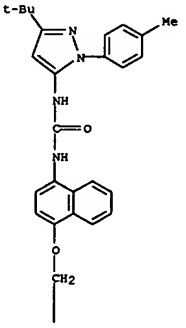
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy for treatment of immunoinflammatory disorders)

RN 285983-48-4 CAPLUS

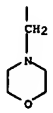
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



L7 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



L7 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:701815 CAPLUS
DOCUMENT NUMBER: 141:185104
TITLE: Compositions, combinations, and methods for treating cardiovascular conditions and other associated conditions
INVENTOR(S): Rudolph, Amy E.; Rocha, Ricardo; Carretero, Oscar
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 107 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167197	A1	20040826	US 2004-788220	20040226
WO 2004075852	A2	20040910	WO 2004-US5609	20040226
WO 2004075852	A3	20050728		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004075857	A2	20040910	WO 2004-US5799	20040226
WO 2004075857	A3	20050818		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005203072	A1	20050915	US 2004-787721	20040226

PRIORITY APPLN. INFO.: US 2003-450529P P 20030226

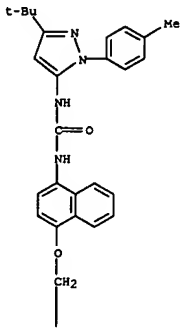
AB This invention is directed generally to a method for treating a pathol. condition (particularly a cardiovascular condition (e.g., hypertension or heart failure) or a condition associated with a cardiovascular condition) using a p38-kinase inhibitor (e.g., a p38-kinase-inhibiting substituted pyrazole), and specifically a combination comprising a p38-kinase inhibitor with an angiotensin-converting-enzyme inhibitor (or "ACE inhibitor") for treating a cardiovascular condition. This invention also is directed generally to combinations comprising a p38-kinase inhibitor, and specifically to combinations comprising a p38-kinase inhibitor with an angiotensin-converting-enzyme inhibitor. This invention is further directed generally to pharmaceutical compns. comprising a p38-kinase

L7 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

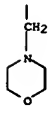
inhibitor, and more specifically to compns. comprising the above-described combinations.

IT **285983-48-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns., combinations, and methods for treating cardiovascular conditions and other associated conditions)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L7 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

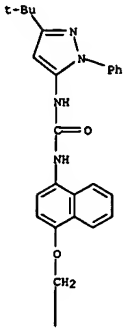
ACCESSION NUMBER: 2004:690875 CAPLUS
DOCUMENT NUMBER: 141:345501
TITLE: Discovery and Characterization of a Substrate Selective p38α Inhibitor
AUTHOR(S): Davidson, Walter; Frego, Lee; Peet, Gregory W.; Kroe, Rachel R.; Labadia, Mark E.; Lukas, Susan M.; Snow, Roger J.; Jakes, Scott; Grygon, Christine A.; Pargellis, Christopher; Werneburg, Brian G.
CORPORATE SOURCE: Department of Immunology and Inflammation, Research and Development Center, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Biochemistry (2004), 43(37), 11658-11671
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel inhibitor of p38 mitogen-activated protein kinase (p38), CMPD1, identified by high-throughput screening, is characterized herein. Unlike the p38 inhibitors described previously, this inhibitor is substrate selective and noncompetitive with ATP. In steady-state kinetics expts., CMPD1 was observed to prevent the p38α-dependent phosphorylation (Kiapp = 330 nM) of the splice variant of mitogen-activated protein kinase-activated protein kinase 2 (MK2a) that contains a docking domain for p38α and p38β, but it did not prevent the phosphorylation of ATF-2 (Kiapp > 20 μM). In addition to kinetic studies, isothermal titration calorimetry and surface plasmon resonance expts. were performed to elucidate the mechanism of inhibition. While isothermal titration calorimetry anal. indicated that CMPD1 binds to p38α, CMPD1 was not observed to compete with ATP for p38α, nor was it able to interrupt the binding of p38α to MK2a observed by surface plasmon resonance. Therefore, deuterium exchange mass spectrometry (DXMS) was employed to study the p38α·CMPD1 inhibitory complex, to provide new insight into the mechanism of substrate selective inhibition. The DXMS data obtained for the p38α·CMPD1 complex were compared to the data obtained for the p38α·MK2a complex and a p38α·active site binding inhibitor complex. Alterations in the DXMS behavior of both p38α and MK2a were observed upon complex formation, including but not limited to the interaction between the carboxy-terminal docking domain of MK2a and its binding groove on p38α. Alterations in the D2O exchange of p38α produced by CMPD1 suggest that the substrate selective inhibitor binds in the vicinity of the active site of p38α, resulting in perturbations to regions containing nucleotide binding pocket residues, docking groove residues (E160 and D161), and a Mg2+ ion cofactor binding residue (D168). Although the exact mechanism of substrate selective inhibition by this novel inhibitor has not yet been disclosed, the results suggest that CMPD1 binding in the active site region of p38α induces perturbations that may result in the suboptimal positioning of substrates and cofactors in the transition state, resulting in selective inhibition of p38α activity.

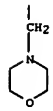
IT **451480-54-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; discovery and characterization of a substrate selective p38α kinase inhibitor)
RN 451480-54-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:262323 CAPLUS
DOCUMENT NUMBER: 141:116347
TITLE: Nuclear Export Inhibitors and Kinase Inhibitors Identified Using a MAPK-Activated Protein Kinase 2 Redistribution Screen
AUTHOR(S): Almholt, Dorthe L. C.; Loechel, Frosty; Nielsen, Soren
J.; Krog-Jensen, Christian; Terry, Robert; Bjorn, Sara
P.; Pedersen, Hans C.; Praestegaard, Morten; Moller, Soren; Heide, Morten; Pagliaro, Len; Mason, Anthony J.; Butcher, Steven; Dahl, Soren W.
CORPORATE SOURCE: BioImage A/S, Soborg, Den.
SOURCE: Assay and Drug Development Technologies (2004), 2(1), 7-20
CODEN: ADDTAR; ISSN: 1540-658X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

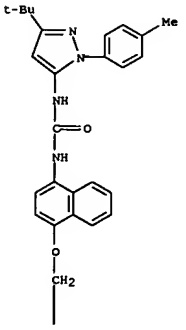
AB Redistribution (BioImage A/S, Soborg, Denmark) is a novel high-throughput screening technol. that monitors translocation of specific protein components of intracellular signaling pathways within intact mammalian cells, using green fluorescent protein as a tag. A single Redistribution assay can be used to identify multiple classes of compds. that act at, or upstream of, the level of the protein target used in the primary screening assay. Such compds. may include both conventional and allosteric enzyme inhibitors, as well as protein-protein interaction modulators. We have developed a series of Redistribution assays to discover and characterize compds. that inhibit tumor necrosis factor-α biosynthesis via modulation of the p38 mitogen-activated protein kinase (MAPK) pathway. A primary assay was designed to identify low-mol.-weight compds. that inhibit the activation-dependent nuclear export of the p38 kinase substrate MAPK-activated protein kinase 2 (MK2). Hits from the primary screen were categorized, using secondary assays, either as direct inhibitors of MK2 nuclear export, or as inhibitors of the upstream p38 MAPK pathway. Activity profiles are presented for a nuclear export inhibitor, and a compound that structurally and functionally resembles a known p38 kinase inhibitor. These results demonstrate the utility of Redistribution technol. as a pathway screening method for the identification of diverse and novel compds. that are active within therapeutically important signaling pathways.

IT 285983-48-4, BIRB796
RL: ANT (Analyte); ANST (Analytical study)
(nuclear export inhibitors and kinase inhibitors identified using MAPK-activated protein kinase 2 Redistribution screen)

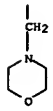
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

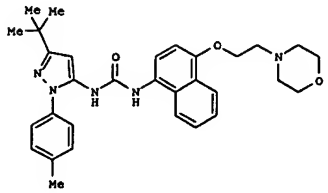
L7 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:142968 CAPLUS
DOCUMENT NUMBER: 140:193056
TITLE: Combinations of active agents with p38 MAP kinase inhibitors, pharmaceutical compositions, and use in the treatment of cytokine-mediated diseases
INVENTOR(S): Simianer, Stefan; Bilbault, Pascal; Cappola, Michael L.; Way, Susan Lynn
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA; Boehringer Ingelheim France
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014387	A1	20040219	WO 2003-US25341	20030812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004110755	A1	20040610	US 2003-638702	20030811
CA 2497448	AA	20040219	CA 2003-2497448	20030812
AU 2003256410	A1	20040225	AU 2003-256410	20030812
EP 1530477	A1	20050518	EP 2003-785255	20030812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006501218	T2	20060112	JP 2004-528105	20030812

PRIORITY APPLN. INFO.:
US 2002-403115P P 20020813
WO 2003-US25341 W 20030812

GI



I

L7 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

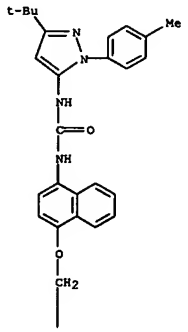
AB The invention relates to pharmaceutical combination therapies based on p38
kinase inhibitors and another active ingredients, pharmaceutical compns. comprising such combinations, processes for preparing them, and their use in
the treatment of cytokine-mediated diseases. Preparation of I (BIRB 796 BS) is
described.

IT **285983-48-4P**, BIRB 796BS
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combinations of active agents with p38 MAP kinase inhibitors, pharmaceutical compns., and use in treatment of cytokine-mediated diseases)

RN 285983-48-4 CAPLUS

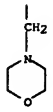
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



L7 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:142601 CAPLUS
DOCUMENT NUMBER: 140:193063
TITLE: Anticoagulant and fibrinolytic therapy using p38 MAP kinase inhibitors
INVENTOR(S): Wood, Chester C.; Van Der Poll, Tom
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., Germany; Boehringer Ingelheim Pharma GmbH & Co. KG
SOURCE: U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004033222	A1	20040219	US 2003-630599	20030730
CA 2496445	AA	20040226	CA 2003-2496445	20030730
WO 2004016267	A1	20040226	WO 2003-US23841	20030730
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003257043	A1	20040303	AU 2003-257043	20030730
EP 1545514	A1	20050629	EP 2003-788293	20030730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006500365	T2	20060105	JP 2004-529211	20030730
US 2005159417	A1	20050721	US 2004-9480	20041210
PRIORITY APPLN. INFO.:			US 2002-403422P P	20020814
			US 2003-630599 B1	20030730
			WO 2003-US23841 W	20030730

AB Disclosed are methods for a treating a disease or condition relating to blood coagulation and fibrinolysis using p38 MAP kinase inhibitors. 1-(3-Tert-butyl-1-p-tolyl-1H-pyrazol-5-yl)-3-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]urea, preparation given, was tested in humans.

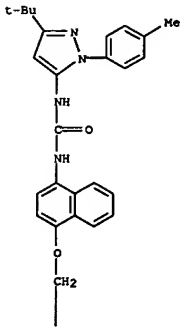
IT **285983-48-4P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(as p38 MAP kinase inhibitor; anticoagulant and fibrinolytic therapy with p38 MAP kinase inhibitors)

RN 285983-48-4 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as p38 MAP kinase inhibitor; anticoagulant and fibrinolytic therapy with p38 MAP kinase inhibitors

L7 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:41274 CAPLUS
DOCUMENT NUMBER: 140:99644
TITLE: Pharmaceutical compositions based on novel anticholinergics and p38 kinase inhibitors
INVENTOR(S): Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004725	A2	20040115	WO 2003-EP6739	20030626
WO 2004004725	A3	20040527		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492033	AA	20040115	CA 2003-2492033	20030626
AU 2003245989	A1	20040123	AU 2003-245989	20030626
EP 1534282	A2	20050601	EP 2003-738089	20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538066	T2	20051215	JP 2004-518584	20030626
US 2004044020	A1	20040304	US 2003-611717	20030701
US 2005163726	A1	20050728	US 2005-68204	20050228

PRIORITY APPLN. INFO.:
EP 2002-15231 A 20020709
US 2002-407733P P 20020903
WO 2003-EP6739 W 20030626
US 2003-611717 A1 20030701

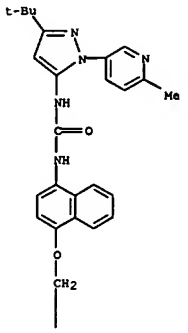
OTHER SOURCE(S): MARPAT 140:99644
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

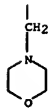
AB The present invention relates to novel pharmaceutical compns. based on novel anticholinergics and p38 kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Inhalation powders were prepared containing anticholinergic I and p38 kinase inhibitor II.
IT **285983-49-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L7 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(pharmaceutical compns. based on novel anticholinergics and p38 kinase inhibitors)
RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L7 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:818288 CAPLUS
DOCUMENT NUMBER: 139:312463
TITLE: New pharmaceutical compositions based on anticholinergics and p38 kinase inhibitors
INVENTOR(S): Jung, Birgit; Pairet, Michel; Pieper, Michael P.; Reiser, Hans Clemens
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany; Boehringer Ingelheim Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

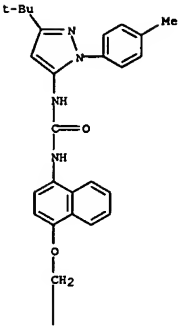
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084539	A2	20031016	WO 2003-EP3624	20030408
WO 2003084539	A3	20040902		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003225089	A1	20031204	US 2003-408718	20030407
CA 2479522	AA	20031016	CA 2003-2479522	20030408
AU 2003224048	A1	20031020	AU 2003-224048	20030408
EP 1496900	A2	20050119	EP 2003-720433	20030408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009099	A	20050329	BR 2003-9099	20030408
CN 1658873	A	20050824	CN 2003-813421	20030408
JP 2005529098	T2	20050929	JP 2003-581779	20030408

PRIORITY APPLN. INFO.:
US 2002-371514P P 20020410
WO 2003-EP3624 W 20030408

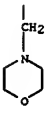
OTHER SOURCE(S): MARPAT 139:312463
AB The present invention relates to novel pharmaceutical compns. based on anticholinergics and p38 kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. For example, inhalatable powders comprised tiotropium bromide (as anticholinergic) 10.8, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]urea (as p38 kinase inhibitor) 3500, and lactose 3489.2 μg per capsule.
IT **285983-48-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. based on anticholinergics and p38 kinase inhibitors for treatment of respiratory diseases)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L7 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

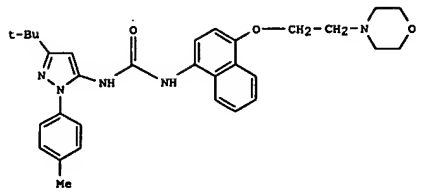
ACCESSION NUMBER: 2003:818257 CAPLUS
DOCUMENT NUMBER: 139:312451
TITLE: Inhalant p38 kinase inhibitor formulations for treating mucus hypersecretion
INVENTOR(S): Jung, Birgit
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084503	A2	20031016	WO 2003-EP3434	20030402
WO 2003084503	A3	20040408		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003220336	A1	20031127	US 2003-400421	20030327
CA 2479520	AA	20031016	CA 2003-2479520	20030402
AU 2003224025	A1	20031020	AU 2003-224025	20030402
EP 1494645	A2	20050112	EP 2003-720407	20030402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009009	A	20050322	BR 2003-9009	20030402
CN 1658834	A	20050824	CN 2003-812988	20030402
JP 2005528374	T2	20050922	JP 2003-581743	20030402

PRIORITY APPLN. INFO.:	EP 2002-7699	A	20020405
	US 2002-385856P	P	20020605
	WO 2003-EP3434	W	20030402

OTHER SOURCE(S): MARPAT 139:312451
GI

L7 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



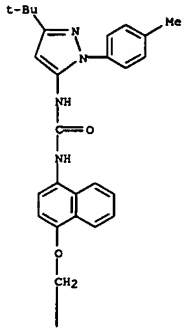
I

AB The invention relates to the use of p38 kinase inhibitors for the preparation of a pharmaceutical composition suitable for inhalation for the treatment of mucus hypersecretion. Furthermore the invention is directed to pharmaceutical compns. suitable for inhalation comprising p38 kinase inhibitors such as I and methods for their preparation

IT 285983-48-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalant p38 kinase inhibitor formulations for treating mucus hypersecretion)

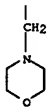
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



L7 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A



L7 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

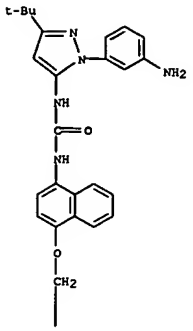
ACCESSION NUMBER: 2003:738975 CAPLUS
DOCUMENT NUMBER: 139:301299
TITLE: Structure-Activity Relationships of the p38α MAP Kinase Inhibitor 1-(5-tert-Butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl]urea (BIRB 796)
AUTHOR(S): Regan, John; Capolino, Alison; Cirillo, Pier F.; Gilmore, Thomas; Graham, Anne G.; Hickey, Eugene; Kroe, Rachel R.; Madwed, Jeffrey; Moriak, Monica; Nelson, Richard; Pargellis, Christopher A.; Swinamer, Alan; Torcellini, Carol; Tsang, Michele; Moss, Neil
CORPORATE SOURCE: Research and Development Center, Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4676-4686
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:301299

AB We report on the structure-activity relationships (SAR) of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naphthalen-1-yl]urea (BIRB 796), an inhibitor of p38α MAP kinase which has advanced into human clin. trials for the treatment of autoimmune diseases. Thermal denaturation was used to establish mol. binding affinities for this class of p38α inhibitors. The tert-Bu group remains a critical binding element by occupying a lipophilic domain in the kinase which is exposed upon rearrangement of the activation loop. An aromatic ring attached to N-2 of the pyrazole nucleus provides important π-CH2 interactions with the kinase. The role of groups attached through an ethoxy group to the 4-position of the naphthalene and directed into the ATP-binding domain is elucidated. Pharmacophores with good hydrogen bonding potential, such as morpholine, pyridine, and imidazole, shift the melting temperature of p38α by 16-17° translating into Kd values of 50-100 pM. Finally, we describe several compds. that potently inhibit TNF-α production when dosed orally in mice.

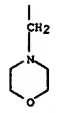
IT 611168-76-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and p38α kinase-inhibiting activity of BIRB 796 analogs for treatment of autoimmune diseases)

RN 611168-76-4 CAPLUS
CN Urea, N-[1-(3-aminophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



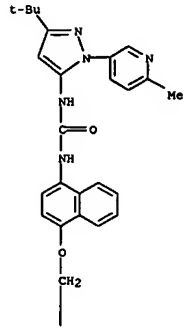
PAGE 2-A



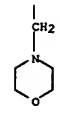
IT **285983-49-5P 285983-51-9P 285983-56-4P**
285983-68-8P 285983-95-1P 285984-06-7P
451480-54-9P 611168-73-1P 611168-74-2P
611168-75-3P 611168-77-5P 611168-78-6P
611168-79-7P 611168-81-1P 611168-82-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and p38α kinase-inhibiting activity of BIRB 796 analogs for treatment of autoimmune diseases)

RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

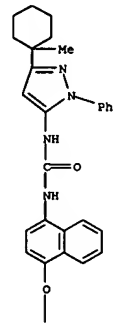


PAGE 2-A

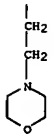


RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

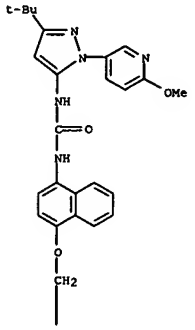


PAGE 2-A

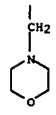


RN 285983-56-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

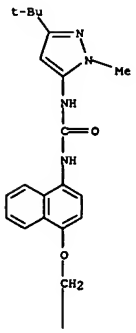


PAGE 2-A

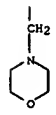


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

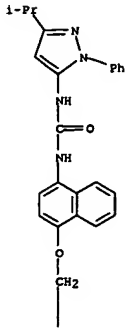


PAGE 2-A

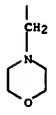


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

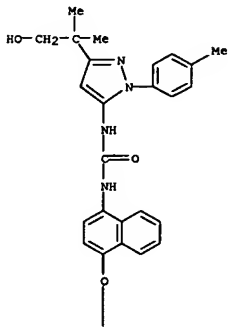


PAGE 2-A

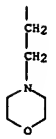


RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

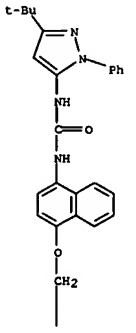


PAGE 2-A

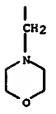


RN 451480-54-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

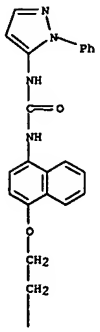


PAGE 2-A



RN 611168-73-1 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-(1-phenyl-1H-pyrazol-5-yl)- (9CI) (CA INDEX NAME)

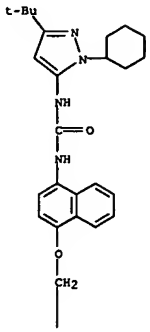
PAGE 1-A



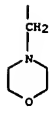
PAGE 2-A

RN 611168-74-2 CAPLUS
CN Urea, N-[1-cyclohexyl-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

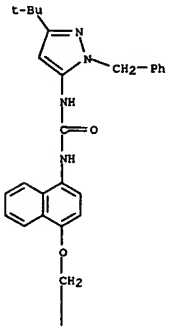


PAGE 2-A

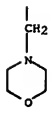


RN 611168-75-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(phenylmethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

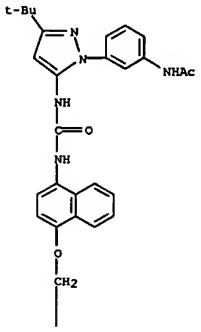


PAGE 2-A

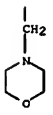


RN 611168-77-5 CAPLUS
CN Acetamide, N-[3-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

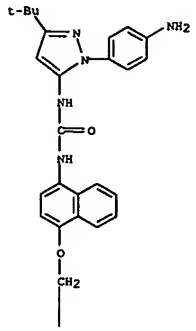


PAGE 2-A

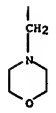


RN 611168-78-6 CAPLUS
CN Urea, N-[1-(4-aminophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

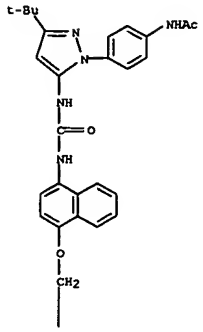


PAGE 2-A

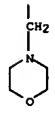


RN 611168-79-7 CAPLUS
CN Acetamide,
N-[4-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



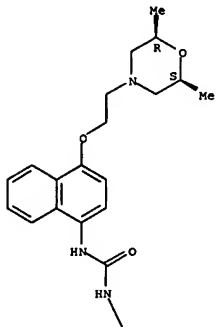
PAGE 2-A



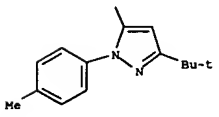
RN 611168-81-1 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2S,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



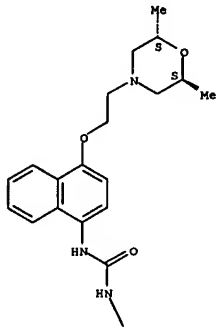
PAGE 2-A



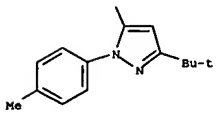
RN 611168-82-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2S,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

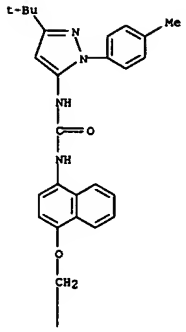


PAGE 2-A

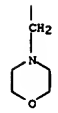


IT 285983-48-4, BIRB 796
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and p38α kinase-inhibiting activity of BIRB 796 analogs for treatment of autoimmune diseases)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

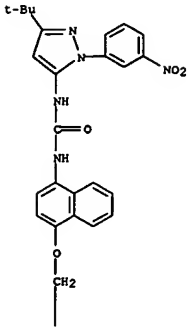


PAGE 2-A

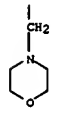


IT 611168-85-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and p38α kinase-inhibiting activity of BIRB 796 analogs for treatment of autoimmune diseases)
RN 611168-85-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-nitrophenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

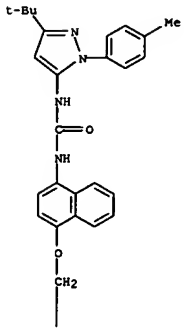
L7 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:738972 CAPLUS
DOCUMENT NUMBER: 139:374260
TITLE: Thermal Denaturation: A Method to Rank Slow Binding, High-Affinity P38α MAP Kinase Inhibitors
AUTHOR(S): Kroe, Rachel R.; Regan, John; Proto, Al; Peet, Gregory W.; Roy, Tapon; Landro, Laura D.; Fuschetto, Natalie G.; Pargellis, Christopher A.; Ingraham, Richard H.
CORPORATE SOURCE: Department of Immunology and Inflammation, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(22), 4669-4675
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

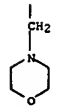
AB It has been reported that the diaryl urea class of p38α inhibitors binds to p38 map kinase with both high affinity and slow binding kinetics (Pargellis et al. Nat. Struct. Biol. 2002, 9, 268-272). The slow binding kinetics of this class of inhibitors is believed to be the result of binding to an allosteric pocket adjacent to the p38α active site. The use of traditional kinetic and equilibrium methods to measure the binding affinity of this class of compds. has created many challenges for determination of structure-activity relationships (SAR). The thermal denaturation method provides a means of measuring high-affinity interactions. In this paper, the method of thermal denaturation will be described as it has been applied to the diaryl urea class of p38 map kinase inhibitors.

IT 285983-48-4 285983-49-5 285983-68-8 285983-95-1 285984-06-7 451480-54-9 611168-73-1
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(thermal denaturation as method to rank slow binding high-affinity P38α MAP kinase inhibitors)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

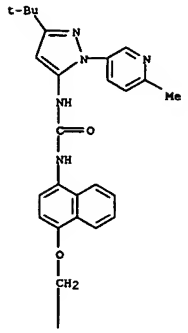


PAGE 2-A

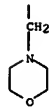


RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

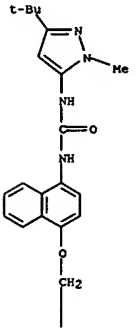


PAGE 2-A

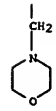


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

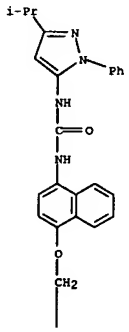


PAGE 2-A

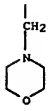


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

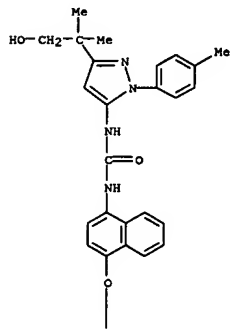


PAGE 2-A

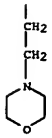


RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

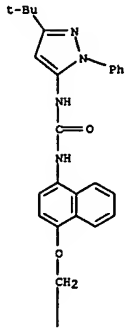


PAGE 2-A

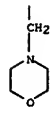


RN 451480-54-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

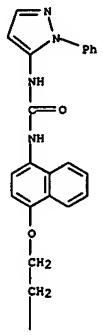


PAGE 2-A



RN 611168-73-1 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-(1-phenyl-1H-pyrazol-5-yl)- (9CI) (CA INDEX NAME)

PAGE 1-A



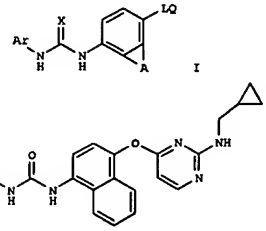
PAGE 2-A

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:696888 CAPLUS
DOCUMENT NUMBER: 139:230482
TITLE: Preparation of 1,4-disubstituted benzofused cycloalkyl
urea compounds useful in treating cytokine mediated diseases
INVENTOR(S): Cirillo, Pier F.; Regan, John R.; Hammach, Abdelhakim
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072569	A1	20030904	WO 2003-US7268	20030219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473634	AA	20030904	CA 2003-2473634	20030219
AU 2003213806	A1	20030909	AU 2003-213806	20030219
US 2003232865	A1	20031218	US 2003-369847	20030219
US 7041669	B2	20060509		
EP 1480973	A1	20041201	EP 2003-711498	20030219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005518447	T2	20050623	JP 2003-571275	20030219
PRIORITY APPLN. INFO.:			US 2002-359809P P	20020225
			WO 2003-US7268 W	20030219

OTHER SOURCE(S): MARPAT 139:230482
GI

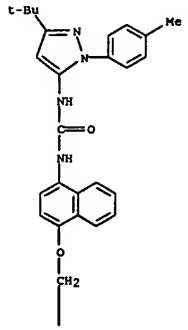


I

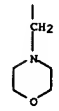
II

AB Benzo-fused urea compds. of formula I [A = (substituted) alkylene; Ar = pyrrole, pyrrolidine, pyrazole, imidazole, oxazole, thiazole, furan, thiophene; L = O, S, NH, alkylene, etc.; Q = Ph, pyridine, pyrimidine, imidazole, furan, pyran, morpholine, etc.; X = O, S] are prepared The compds. inhibit production of cytokines involved in inflammatory processes and
are thus useful for treating diseases and pathol. conditions involving inflammation such as chronic inflammatory disease. Also disclosed are processes for preparing these compds. and compns., and pharmaceutical compns.
comprising these compds. Thus, II was prepared from 4-amino-1-naphthol hydrochloride, 2,4-dichloropyrimidine, cyclopropanemethylamine and 5-amino-3-tert-butyl-1-methylpyrazole.
IT **285983-48-4P 285983-49-5P 285983-68-8P**
591772-78-0P 591772-80-4P 591772-82-6P
591772-83-7P 591772-84-8P 591772-86-0P
591772-88-2P 591772-90-6P 591772-92-8P
591772-94-0P 591772-96-2P 591772-98-4P
591773-00-1P 591773-02-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzo-fused cycloalkyl urea compds. as inhibitors of cytokine production)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

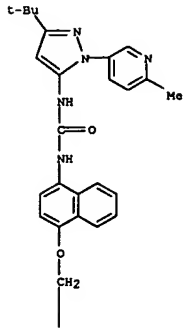


PAGE 2-A

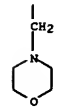


RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

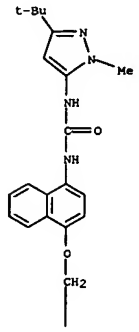


PAGE 2-A

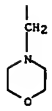


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

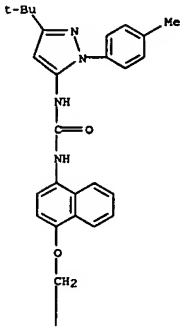


PAGE 2-A

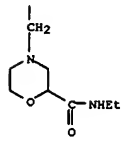


RN 591772-78-0 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N-ethyl- (9CI) (CA INDEX NAME)

PAGE 1-A

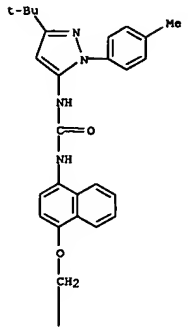


PAGE 2-A

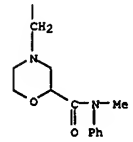


RN 591772-80-4 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N-methyl-N-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A

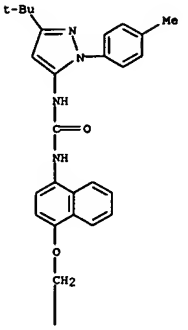


PAGE 2-A

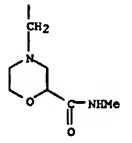


RN 591772-82-6 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

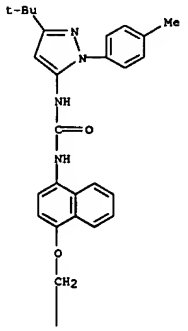


PAGE 2-A

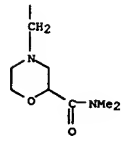


RN 591772-83-7 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

PAGE 1-A

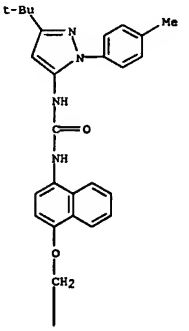


PAGE 2-A

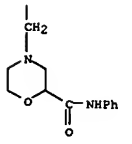


RN 591772-84-8 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A

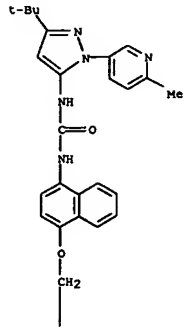


PAGE 2-A

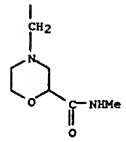


RN 591772-86-0 CAPLUS
CN 2-Morpholinecarboxamide, 4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-N-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A



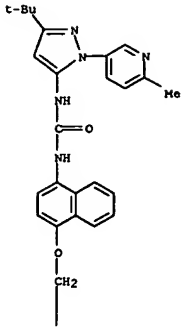
PAGE 2-A



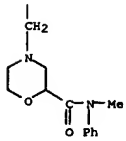
RN 591772-88-2 CAPLUS
CN 2-Morpholinecarboxamide,
4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(6-methyl-3-

pyridinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-
N-methyl-N-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A



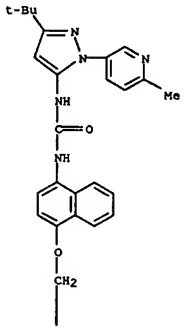
PAGE 2-A



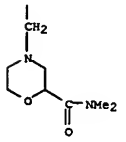
RN 591772-90-6 CAPLUS
CN 2-Morpholinecarboxamide,
4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(6-methyl-3-

pyridinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-
N,N-dimethyl- (9CI) (CA INDEX NAME)

PAGE 1-A



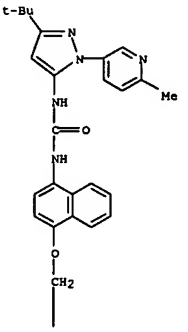
PAGE 2-A



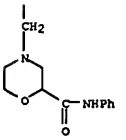
RN 591772-92-8 CAPLUS
CN 2-Morpholinecarboxamide,
4-[2-[[4-[[[[3-(1,1-dimethylethyl)-1-(6-methyl-3-

pyridinyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]ethyl]-
N-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A

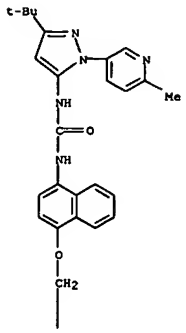


PAGE 2-A

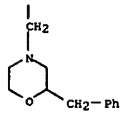


RN 591772-94-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-
N'-[4-[2-[2-(phenylmethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI)
(CA INDEX NAME)

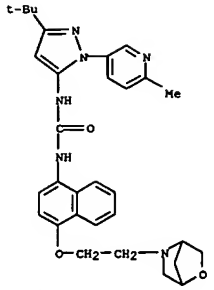
PAGE 1-A



PAGE 2-A

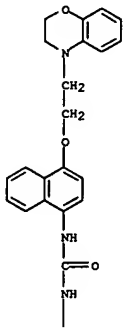


RN 591772-96-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(2-oxa-5-azabicyclo[2.2.1]hept-5-yl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

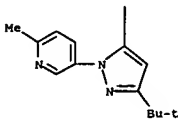


RN 591772-98-4 CAPLUS
CN Urea, N-[4-[2-(2,3-dihydro-4H-1,4-benzoxazin-4-yl)ethoxy]-1-naphthalenyl]-N'-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

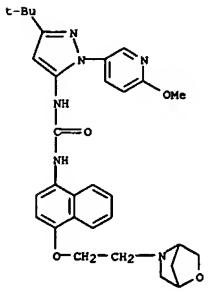
PAGE 1-A



PAGE 2-A

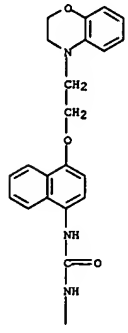


RN 591773-00-1 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(2-oxa-5-azabicyclo[2.2.1]hept-5-yl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

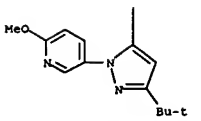


RN 591773-02-3 CAPLUS
CN Urea, N-[4-[2-(2,3-dihydro-4H-1,4-benzoxazin-4-yl)ethoxy]-1-naphthalenyl]-N'-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:665555 CAPLUS
DOCUMENT NUMBER: 139:319154
TITLE: The kinetics of binding to p38 MAP kinase of analogues of BIRB 796
AUTHOR(S): Regan, John; Pargellis, Christopher A.; Cirillo, Pier F.; Gilmore, Thomas; Hickey, Eugene R.; Peet, Gregory W.; Proto, Alfred; Swinamer, Alan; Moss, Neil
CORPORATE SOURCE: Departments of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(18), 3101-3104
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB BIRB 796, a member of the N-pyrazole-N'-naphthyl urea class of p38 MAPK inhibitors, binds to the kinase with both slow association and dissociation rates.

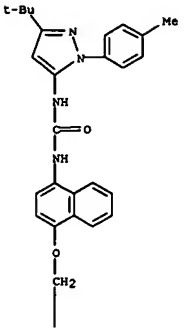
Prior to binding, the kinase undergoes a reorganization of the activation loop exposing a critical binding domain. We demonstrate that, independent of the loop movement, association rates are governed by low energy conformations of the inhibitor and polar functionality on the tolyl ring. As anticipated, the dissociation rates of the inhibitors from the kinase are slowed by lipophilic and hydrogen bond interactions. The value of structure-kinetic relationships (SKR) in drug design is discussed.

IT **285983-48-4**, BIRB 796 **285983-49-5** **285983-68-8** **285983-95-1** **285984-02-3** **285984-03-4** **285984-06-7** **451480-54-9** **611168-73-1** **613222-75-6** **613222-81-4**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(kinetics of p38 MAP kinase binding by BIRB 796 analogs)

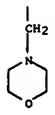
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



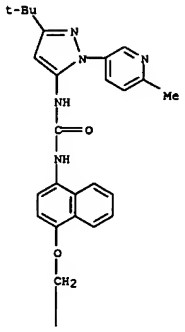
PAGE 2-A



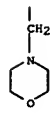
RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



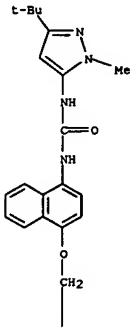
PAGE 2-A



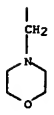
RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

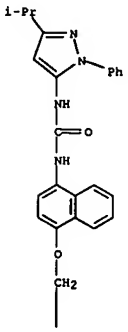


PAGE 2-A

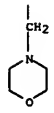


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

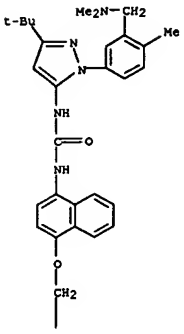


PAGE 2-A

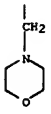


RN 285984-02-3 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]-4-methylphenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

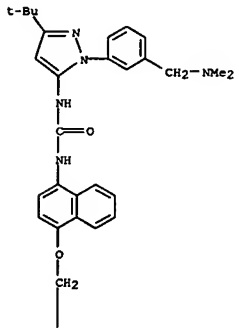


PAGE 2-A

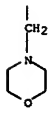


RN 285984-03-4 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]phenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

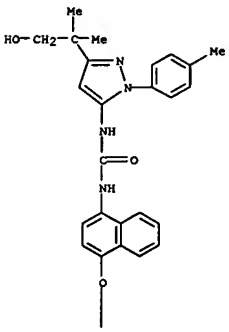


PAGE 2-A

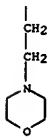


RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

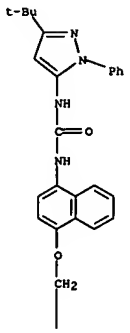


PAGE 2-A

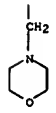


RN 451480-54-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

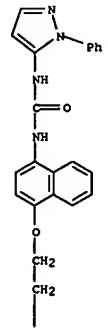


PAGE 2-A



RN 611168-73-1 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-(1-phenyl-1H-pyrazol-5-yl)- (9CI) (CA INDEX NAME)

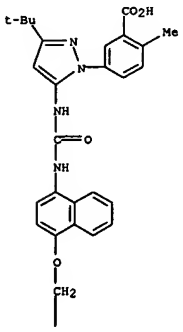
PAGE 1-A



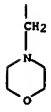
PAGE 2-A

RN 613222-75-6 CAPLUS
CN Benzoic acid, 5-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]-2-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

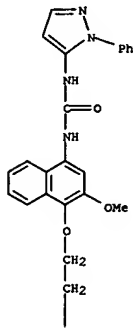


PAGE 2-A



RN 613222-81-4 CAPLUS
CN Urea, N-[3-methoxy-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-(1-phenyl-1H-pyrazol-5-yl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

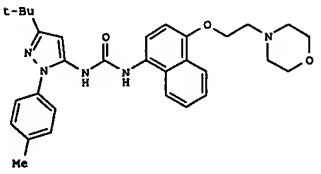
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:656575 CAPLUS
DOCUMENT NUMBER: 139:197476
TITLE: Preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity
INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068223	A1	20030821	WO 2003-US4102	20030211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2003210969	A1	20030904	AU 2003-210969	20030211
US 2004023961	A1	20040205	US 2003-361844	20030211
PRIORITY APPLN. INFO.:			US 2002-354948P	P 20020211
			WO 2003-US4102	W 20030211

GI



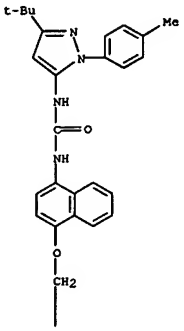
I

AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl)pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy)naphthylamine (prepns. given) and CDI in CH2Cl2 afforded 80% I which showed IC50 of < 1 μM in in vitro raf kinase and in in vitro Flk-1 ELISA assay.

IT 285983-44-0P 285983-47-3P 285983-48-4P
285983-49-5P 285983-51-9P 285983-54-2P
285983-56-4P 285983-57-5P 285983-58-6P
285983-64-4P 285983-68-8P 285983-74-6P
285983-89-3P 285983-90-6P 285983-92-8P
285983-95-1P 285983-96-2P 285983-97-3P
285983-98-4P 285983-99-5P 285984-00-1P
285984-01-2P 285984-02-3P 285984-03-4P
285984-04-5P 285984-06-7P 285984-07-8P
285984-08-9P 285984-09-0P 285984-10-3P
285984-11-4P 285984-12-5P 285984-13-6P
285984-20-5P 285984-21-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

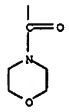
RN 285983-44-0 CAPLUS
CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



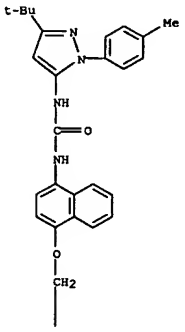
L7 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

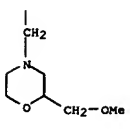


RN 285983-47-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(methoxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



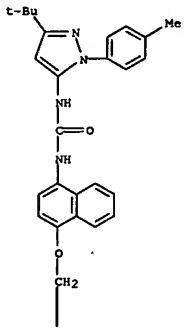
PAGE 2-A



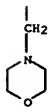
RN 285983-48-4 CAPLUS

L7 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

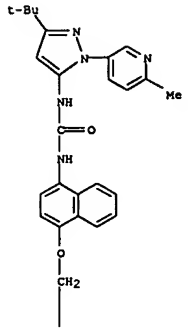


PAGE 2-A

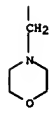


RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

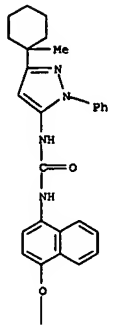


PAGE 2-A

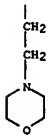


RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

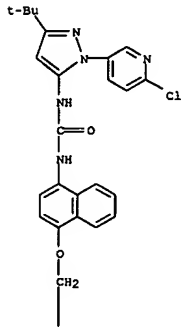


PAGE 2-A

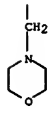


RN 285983-54-2 CAPLUS
CN Urea, N-[1-(6-chloro-3-pyridinyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

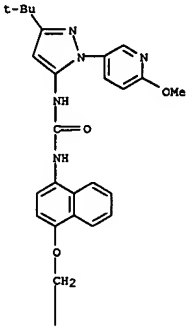


PAGE 2-A

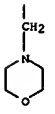


RN 285983-56-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

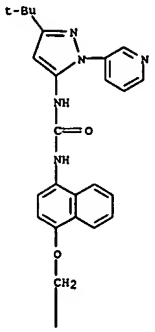


PAGE 2-A

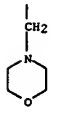


RN 285983-57-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

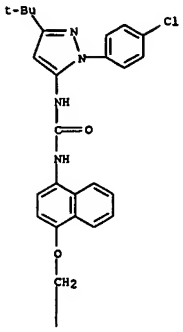


PAGE 2-A

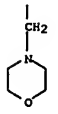


RN 285983-58-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

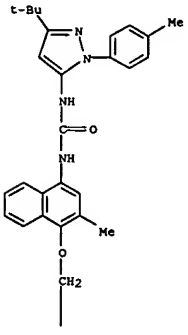


PAGE 2-A

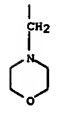


RN 285983-64-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[3-methyl-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

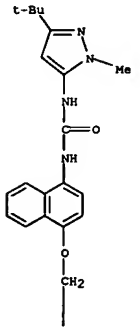


PAGE 2-A

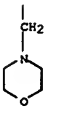


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

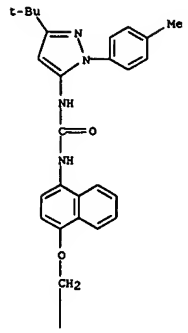


PAGE 2-A

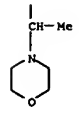


RN 285983-74-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)propoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



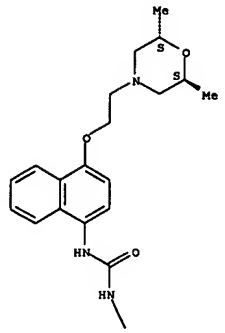
PAGE 2-A



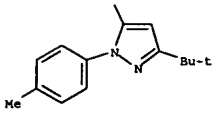
RN 285983-89-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



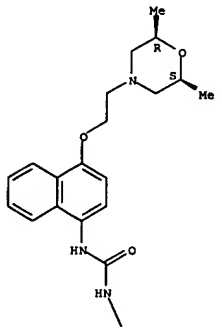
PAGE 2-A



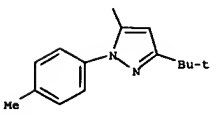
RN 285983-90-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

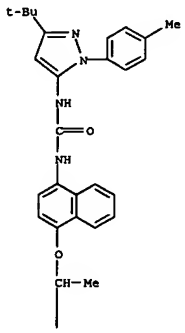


PAGE 2-A

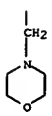


RN 285983-92-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[1-methyl-2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

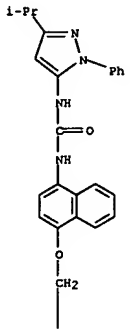


PAGE 2-A

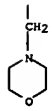


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

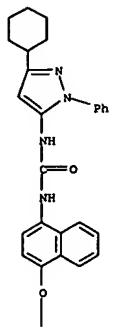


PAGE 2-A

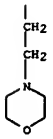


RN 285983-96-2 CAPLUS
CN Urea, N-(3-cyclohexyl-1-phenyl-1H-pyrazol-5-yl)-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

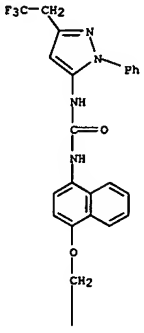


PAGE 2-A

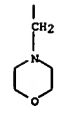


RN 285983-97-3 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-[1-phenyl-3-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

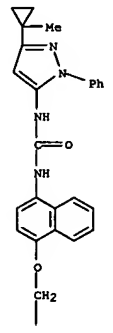


PAGE 2-A

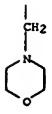


RN 285983-98-4 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

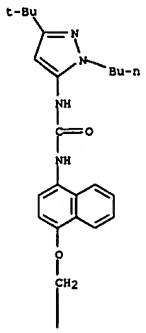


PAGE 2-A

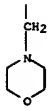


RN 285983-99-5 CAPLUS
CN Urea, N-[1-butyl-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

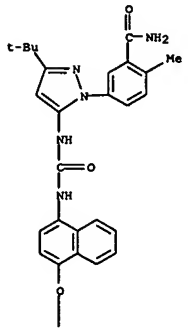


PAGE 2-A

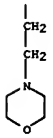


RN 285984-00-1 CAPLUS
CN Benzamide, 5-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]-2-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

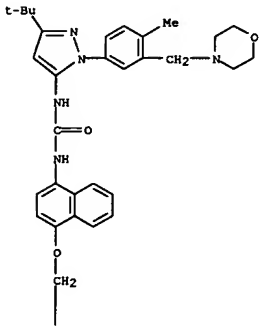


PAGE 2-A

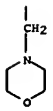


RN 285984-01-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-methyl-3-(4-morpholinylmethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

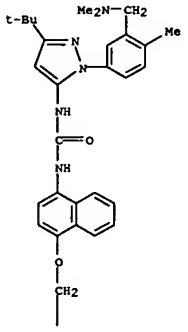


PAGE 2-A

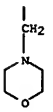


RN 285984-02-3 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]-4-methylphenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

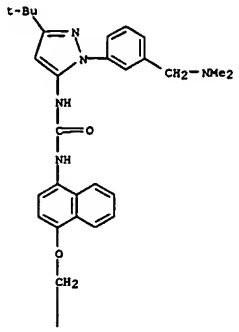


PAGE 2-A

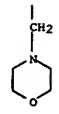


RN 285984-03-4 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]phenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



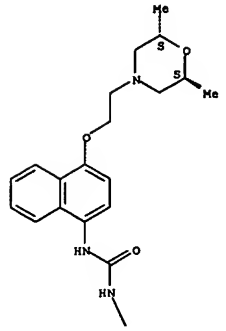
PAGE 2-A



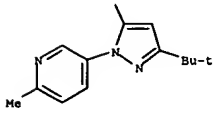
RN 285984-04-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

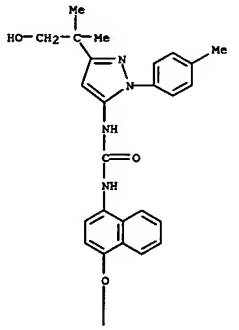


PAGE 2-A

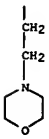


RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

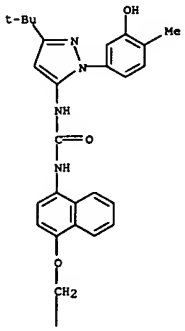


PAGE 2-A

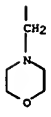


RN 285984-07-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

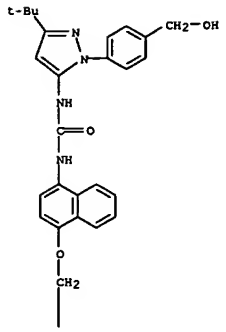


PAGE 2-A

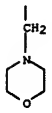


RN 285984-08-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-(hydroxymethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

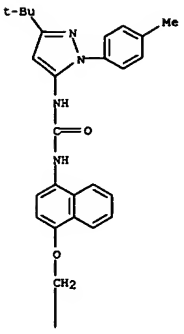


PAGE 2-A

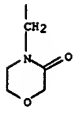


RN 285984-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(3-oxo-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

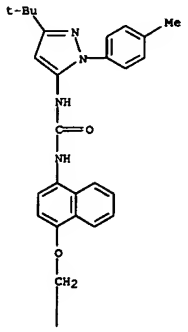


PAGE 2-A

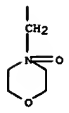


RN 285984-10-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

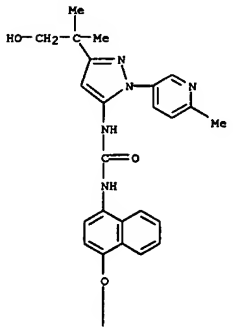


PAGE 2-A

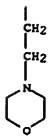


RN 285984-11-4 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

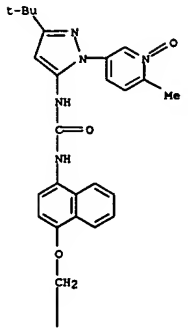


PAGE 2-A

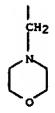


RN 285984-12-5 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-(6-methyl-1-oxido-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

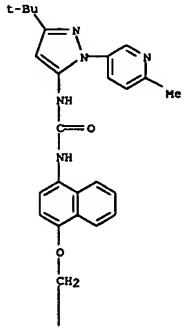


PAGE 2-A

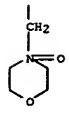


RN 285984-13-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

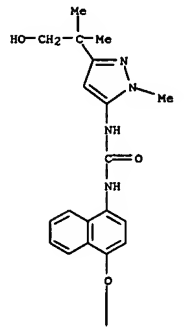


PAGE 2-A

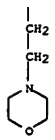


RN 285984-20-5 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

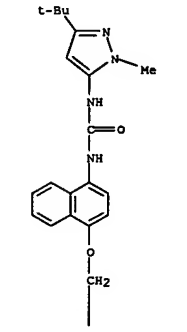


PAGE 2-A

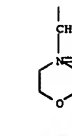


RN 285984-21-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:472391 CAPLUS
DOCUMENT NUMBER: 139:30815
TITLE: Method for administration of BIRB 796 BS for the treatment of human cytokine mediated diseases
INVENTOR(S): Grob, Peter M.; Madwed, Jeffrey B.; Pargellis, Christopher; Yong, Chan Loi
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049742	A1	20030619	WO 2002-US39289	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2465759	AA	20030619	CA 2002-2465759	20021206
AU 2002366644	A1	20030623	AU 2002-366644	20021206
US 2003118575	A1	20030626	US 2002-313667	20021206
EP 1455791	A1	20040915	EP 2002-804546	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005511722	T2	20050428	JP 2003-550791	20021206
PRIORITY APPLN. INFO.:			US 2001-339249P	P 20011211
			WO 2002-US39289	W 20021206

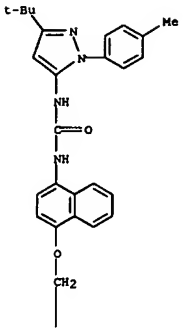
AB Disclosed are methods of administration of BIRB 796 BS, a p38 MAPK inhibitor, at particular dosages for the treatment of human cytokine mediated diseases.

IT **285983-48-4**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for administration of BIRB 796 BS for treatment of human cytokine mediated diseases)

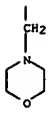
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 47 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:154285 CAPLUS
DOCUMENT NUMBER: 138:193302
TITLE: Parenteral formulations of BIRB 796
INVENTOR(S): Cappola, Michael L.; Way, Susan L.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015828	A1	20030227	WO 2002-US25110	20020808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2454913	AA	20030227	CA 2002-2454913	20020808
US 2003068340	A1	20030410	US 2002-214782	20021021
PRIORITY APPLN. INFO.:			US 2001-313527P	P 20010820
			WO 2002-US25110	W 20020808

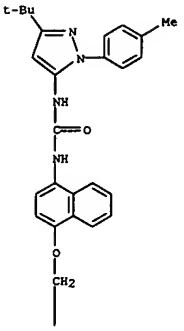
AB Preparation of improved parenteral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphth len-1-yl]-urea (BIRB 796), using an oligosaccharide capable of forming an association or complex with BIRB 796, e.g., a cyclodextrin, are described. Also disclosed are methods of treating cytokine-mediated diseases using such formulations and compns.

IT **285983-48-4**, BIRB 796
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of lyophilized BIRB 796 powder containing oligosaccharide for parenteral formulations)

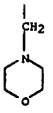
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 48 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

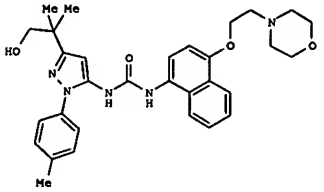
L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:150529 CAPLUS
DOCUMENT NUMBER: 138:205052
TITLE: Preparation of 1-(pyrazol-3-yl)-3-(1-naphthyl)ureas as antiinflammatory agents
INVENTOR(S): Cirillo, Pier Francesco; Dinallo, Roger; Regan, John Robinson; Riska, Paul S.; Swinamer, Alan David; Tan, Zhulin; Walter, Brian Andrew
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 879,776, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6525046	B1	20030225	US 2002-165372	20020607
US 6319921	B1	20011120	US 2000-484638	20000118
US 6333325	B1	20011225	US 2001-871559	20010531
US 2002058678	A1	20020516	US 2001-879776	20010612
US 6329415	B1	20011211	US 2001-891579	20010626
US 2002065285	A1	20020530	US 2001-891820	20010626
US 6506748	B2	20030114		

PRIORITY APPLN. INFO.: US 2000-484638 A3 20000118
US 2001-879776 B2 20010612
US 1999-116400P P 19990119

OTHER SOURCE(S): MARPAT 138:205052
GI



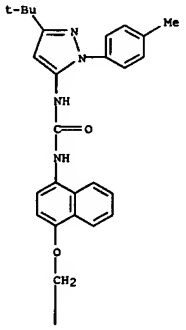
I

AB The title compds. Ar1NHC(:X)NHAr2LQ [Ar1 = pyrazolyl, pyrrolyl, imidazolyl, etc.; Ar2 = Ph, naphthyl, quinolyl, etc.; L = alkylene wherein one or more methylene groups are optionally replaced by O, N or S; Q = Ph, naphthyl, pyridyl, etc.; X = O, S], useful for treating diseases involving inflammation such as chronic inflammatory diseases, were prepd. E.g., a multi-step synthesis of I, starting from Me 2,2-dimethyl-3-hydroxypropionate, was given. Representative title ureas showed IC50 of <10 μM against TNF prodn. in THP cells.

IT 285983-44-0P 285983-47-3P 285983-48-4P
285983-49-5P 285983-51-9P 285983-54-2P
285983-56-4P 285983-57-5P 285983-58-6P
285983-64-4P 285983-68-8P 285983-87-1P
285983-89-3P 285983-90-6P 285984-07-8P
285984-08-9P 285984-10-3P 285984-11-4P
285984-12-5P 285984-13-6P 285984-20-5P
285984-21-6P 476010-09-0P 489432-48-6P
489432-49-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-(pyrazol-3-yl)-3-(1-naphthyl)ureas as antiinflammatory agents)

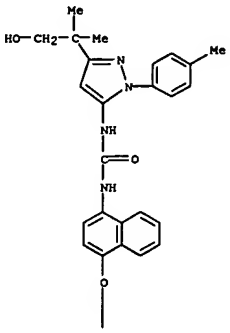
RN 285983-44-0 CAPLUS
CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

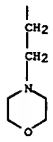


L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

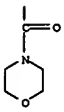


PAGE 2-A



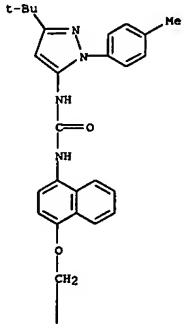
L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

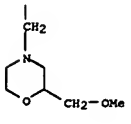


RN 285983-47-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(methoxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



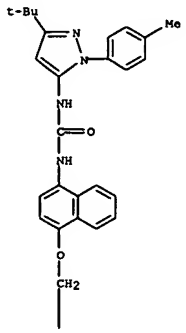
PAGE 2-A



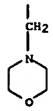
RN 285983-48-4 CAPLUS

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



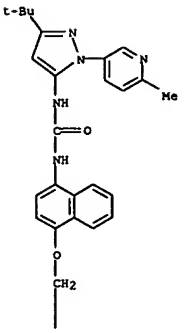
PAGE 2-A



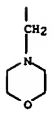
RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



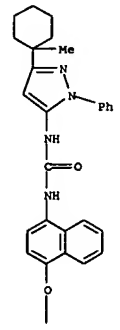
PAGE 2-A



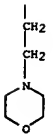
RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



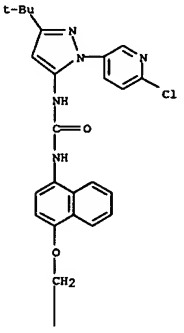
PAGE 2-A



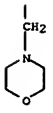
RN 285983-54-2 CAPLUS
CN Urea, N-[1-(6-chloro-3-pyridinyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

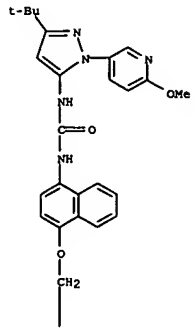


PAGE 2-A

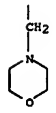


RN 285983-56-4 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

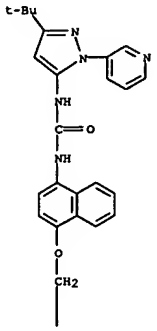


PAGE 2-A

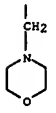


RN 285983-57-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

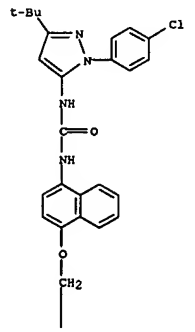


PAGE 2-A

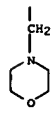


RN 285983-58-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

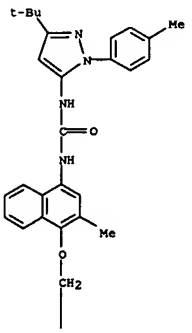


PAGE 2-A

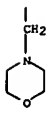


RN 285983-64-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[3-methyl-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

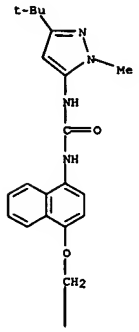


PAGE 2-A

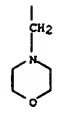


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

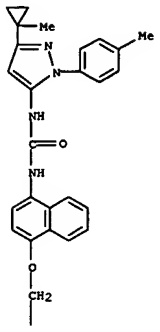


PAGE 2-A

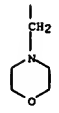


RN 285983-87-1 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



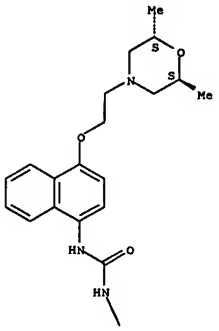
PAGE 2-A



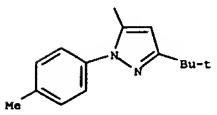
RN 285983-89-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



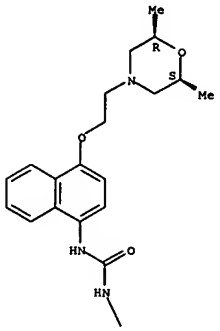
PAGE 2-A



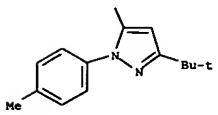
RN 285983-90-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



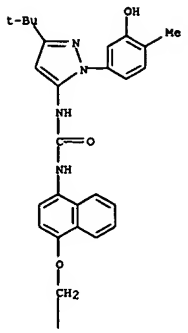
PAGE 2-A



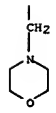
RN 285984-07-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



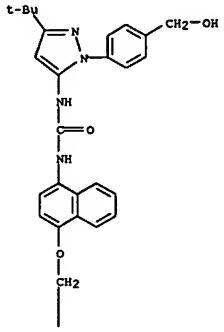
PAGE 2-A



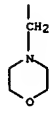
RN 285984-08-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-(hydroxymethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



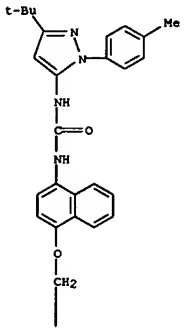
PAGE 2-A



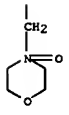
RN 285984-10-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



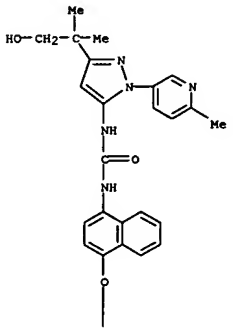
PAGE 2-A



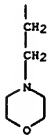
RN 285984-11-4 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 49 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

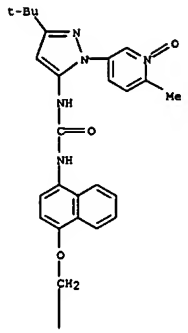


PAGE 2-A

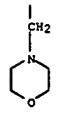


RN 285984-12-5 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-(6-methyl-1-oxido-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

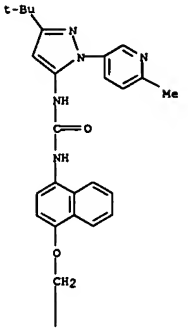


PAGE 2-A

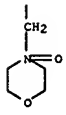


RN 285984-13-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

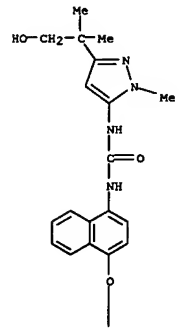


PAGE 2-A

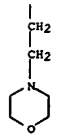


RN 285984-20-5 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

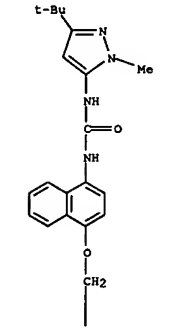


PAGE 2-A

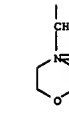


RN 285984-21-6 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

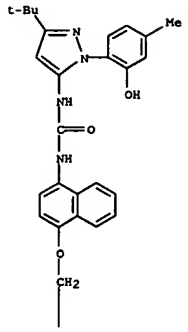


PAGE 2-A

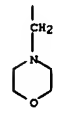


RN 476010-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(2-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

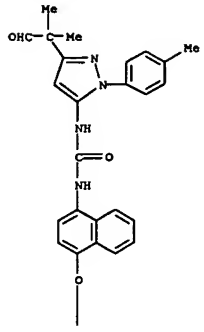


PAGE 2-A

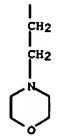


RN 489432-48-6 CAPLUS
CN Urea, N-[3-(1,1-dimethyl-2-oxoethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

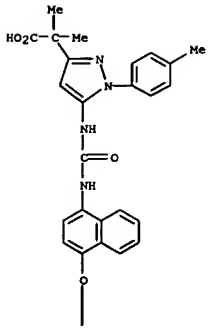


PAGE 2-A

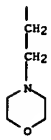


RN 489432-49-7 CAPLUS
CN 1H-Pyrazole-3-acetic acid, α,α-dimethyl-1-(4-methylphenyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

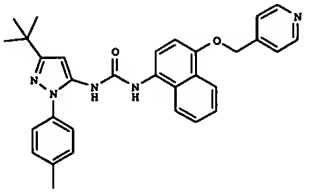
L7 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:57886 CAPLUS
DOCUMENT NUMBER: 138:122641
TITLE: Method of treating cytokine mediated diseases using pyrazolylureas.
INVENTOR(S): Moss, Neil; Regan, John R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003005999	A2	20030123	WO 2002-US20649	20020701
WO 2003005999	A3	20030417		
WO 2003005999	C1	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2453147	AA	20030123	CA 2002-2453147	20020701
US 2003130309	A1	20030710	US 2002-187942	20020701
US 6916814	B2	20050712		
EP 1408950	A2	20040421	EP 2002-746764	20020701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004536845	T2	20041209	JP 2003-511806	20020701
US 2004152725	A1	20040805	US 2004-761913	20040120

PRIORITY APPLN. INFO.: US 2001-304511P P 20010711
US 2002-187942 A3 20020701
WO 2002-US20649 W 20020701

OTHER SOURCE(S): MARPAT 138:122641
GI



I

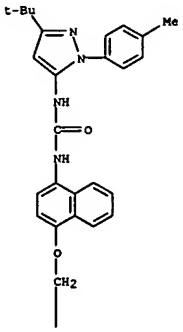
AB A method of treating lung inflammation, endometriosis, behcet's disease, uveitis, ankylosing spondylitis, pancreatitis, cancer, percutaneous transluminal coronary angioplasty, alzheimer's disease, traumatic arthritis, sepsis, chronic obstructive pulmonary disease, and congestive heart failure comprises administration of ArlNHC(:X)NHAr2LQ [Ar1 = (substituted) pyrrolyl, pyrrolidinyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, furyl, thienyl; Ar2 = (substituted) Ph, naphthyl, quinolinyl, isoquinolinyl, tetrahydronaphthyl, tetrahydroisoquinolinyl, benzimidazolyl, benzofuryl, indanyl, indolyl, etc.; L = (O-, S-, or N-interrupted) (unsatd.) (substituted) alkylene; Q = (substituted) Ph, naphthyl, pyridyl, pyrimidinyl, imidazolyl, tetrahydropyranyl, tetrahydrofuryl, dioxanyl, alkoxy, amino, etc.; X = O, S]. Thus, 5-amino-3-tert-butyl-1-(4-methylphenyl)pyrazole was stirred with COCl2 and NaHCO3 in PhMe/CH2Cl2 at 0-5° for 15 min. The organic residue was stirred overnight with 1-amino-4-(4-pyridinylmethoxy)naphthalene dihydrochloride (preparation given) and diisopropylethylamine in THF to give title compound (I). Representative title compds. inhibited TNF production in THP cells with IC50<10 μM.

IT **285983-48-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(method of treating cytokine mediated diseases using pyrazolylureas)

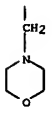
RN 285983-48-4 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

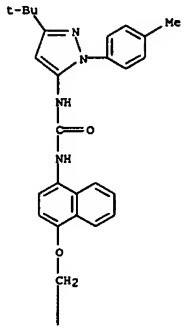


IT **285983-44-0P 285983-47-3P 285983-49-5P**
285983-51-9P 285983-54-2P 285983-56-4P
285983-57-5P 285983-58-6P 285983-64-4P
285983-68-8P 285983-87-1P 285983-89-3P
285983-90-6P 285984-06-7P 285984-07-8P
285984-10-3P 476010-09-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of treating cytokine mediated diseases using pyrazolylureas)

RN 285983-44-0 CAPLUS

CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

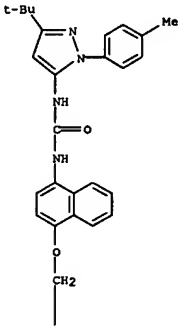


PAGE 2-A

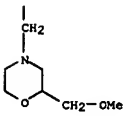
RN 285983-47-3 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(methoxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



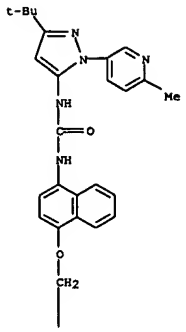
PAGE 2-A



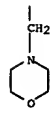
RN 285983-49-5 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

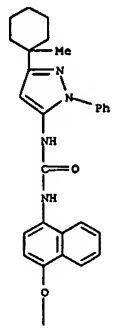


PAGE 2-A

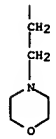


RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

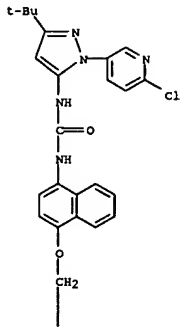


PAGE 2-A

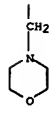


RN 285983-54-2 CAPLUS
CN Urea, N-[1-(6-chloro-3-pyridinyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

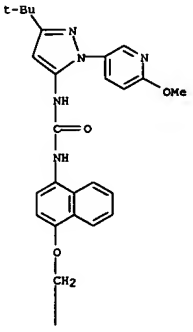


PAGE 2-A

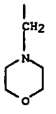


RN 285983-56-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

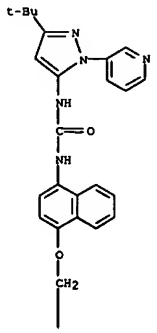


PAGE 2-A

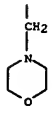


RN 285983-57-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

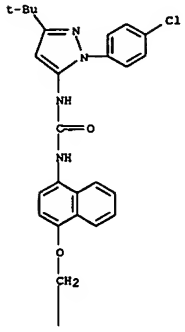


PAGE 2-A

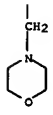


RN 285983-58-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

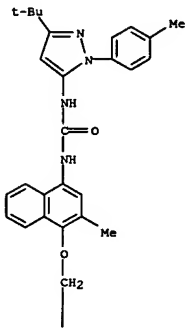


PAGE 2-A

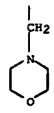


RN 285983-64-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[3-methyl-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

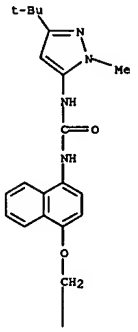


PAGE 2-A

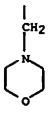


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

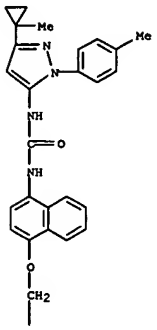


PAGE 2-A

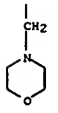


RN 285983-87-1 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



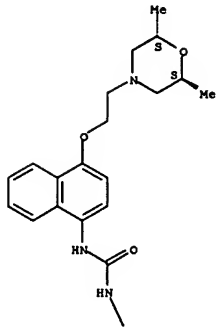
PAGE 2-A



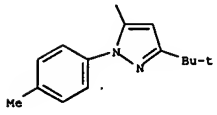
RN 285983-89-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



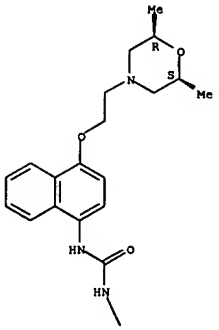
PAGE 2-A



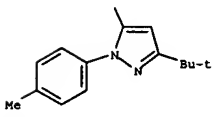
RN 285983-90-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

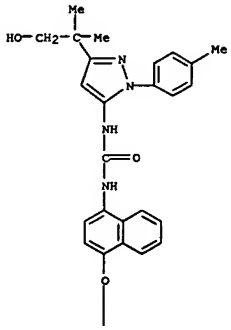


PAGE 2-A

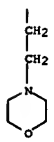


RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

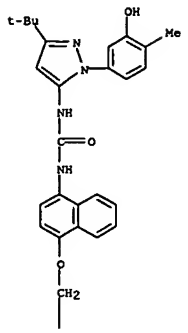


PAGE 2-A

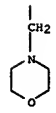


RN 285984-07-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

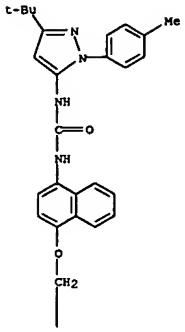


PAGE 2-A

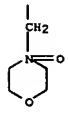


RN 285984-10-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

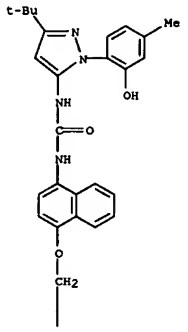


PAGE 2-A

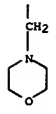


RN 476010-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(2-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



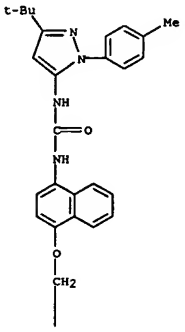
PAGE 2-A



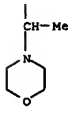
IT 285983-74-6 285983-92-8 285983-95-1
285983-96-2 285983-97-3 285983-98-4
285983-99-5 285984-00-1 285984-01-2
285984-02-3 285984-03-4 285984-04-5
285984-08-9 285984-09-0 285984-11-4
285984-12-5 285984-13-6 285984-20-5
285984-21-6 489432-47-5 489432-48-6
489432-49-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating cytokine mediated diseases using pyrazolylureas)

RN 285983-74-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)propoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

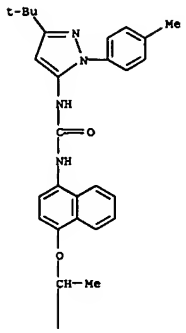


PAGE 2-A

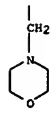


RN 285983-92-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[1-methyl-2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

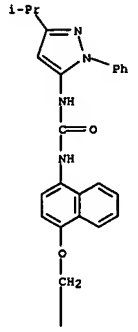


PAGE 2-A

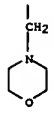


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

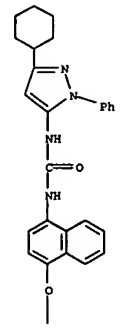


PAGE 2-A

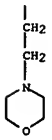


RN 285983-96-2 CAPLUS
CN Urea, N-(3-cyclohexyl-1-phenyl-1H-pyrazol-5-yl)-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

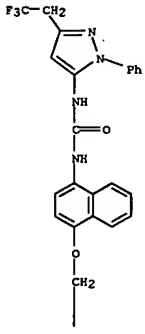


PAGE 2-A

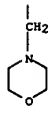


RN 285983-97-3 CAPLUS
CN Urea,
N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-[1-phenyl-3-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

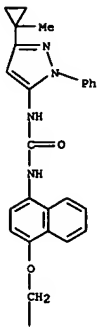


PAGE 2-A

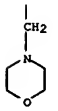


RN 285983-98-4 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

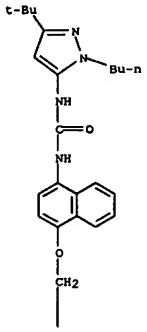


PAGE 2-A

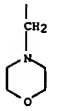


RN 285983-99-5 CAPLUS
CN Urea, N-[1-butyl-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

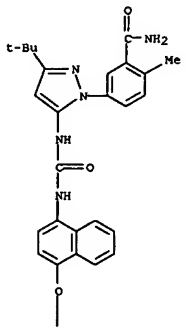


PAGE 2-A

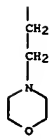


RN 285984-00-1 CAPLUS
CN Benzamide, 5-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]-2-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

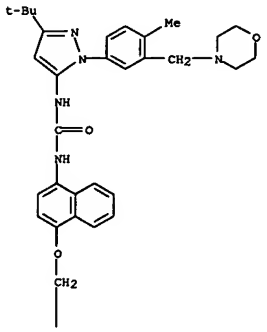


PAGE 2-A

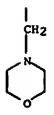


RN 285984-01-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-methyl-3-(4-morpholinylmethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

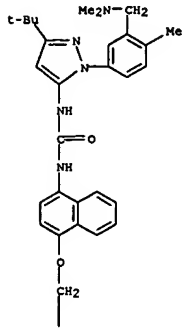


PAGE 2-A

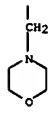


RN 285984-02-3 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]-4-methylphenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

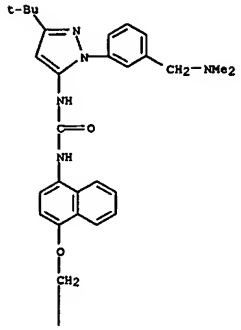


PAGE 2-A

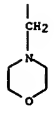


RN 285984-03-4 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]phenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



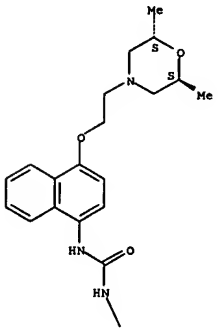
PAGE 2-A



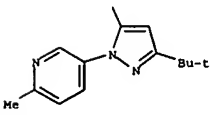
RN 285984-04-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

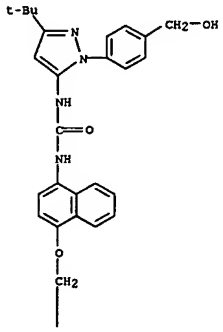


PAGE 2-A

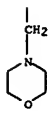


RN 285984-08-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-(hydroxymethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

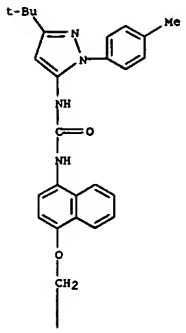


PAGE 2-A

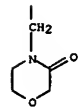


RN 285984-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(3-oxo-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

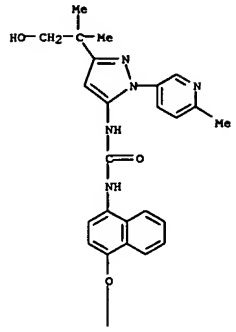


PAGE 2-A

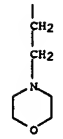


RN 285984-11-4 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

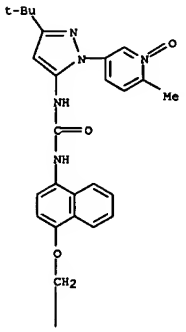


PAGE 2-A

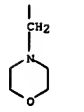


RN 285984-12-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-1-oxido-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

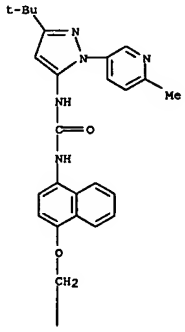


PAGE 2-A

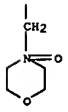


RN 285984-13-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

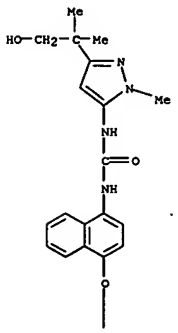


PAGE 2-A

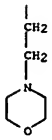


RN 285984-20-5 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

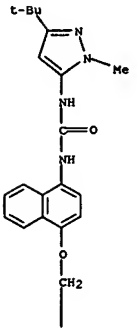


PAGE 2-A

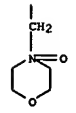


RN 285984-21-6 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

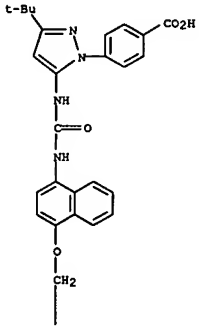


PAGE 2-A

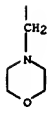


RN 489432-47-5 CAPLUS
CN Benzoic acid,
4-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

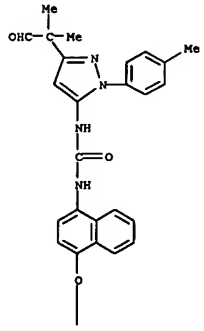


PAGE 2-A

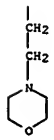


RN 489432-48-6 CAPLUS
CN Urea, N-[3-(1,1-dimethyl-2-oxoethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



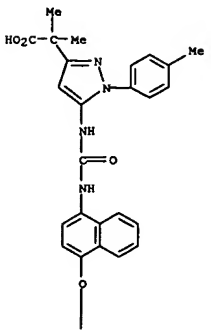
PAGE 2-A



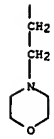
RN 489432-49-7 CAPLUS
CN 1H-Pyrazole-3-acetic acid, α,α-dimethyl-1-(4-methylphenyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

L7 ANSWER 50 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

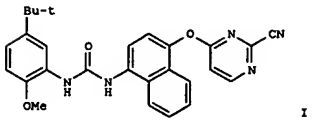


L7 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:888719 CAPLUS
DOCUMENT NUMBER: 137:384854
TITLE: Preparation of diaryl ureas as antiinflammatory agents
INVENTOR(S): Cirillo, Pier F.; Goldberg, Daniel R.; Hammach, Abdelhakim; Moss, Neil; Regan, John Robinson
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092576	A1	20021121	WO 2002-US14733	20020508
W: AE, AU, BG, BR, CA, CN, CO, CZ, EC, EE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2445003	AA	20021121	CA 2002-2445003	20020508
EP 1392661	A1	20040303	EP 2002-734324	20020508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
JP 2004530690	T2	20041007	JP 2002-589462	20020508
US 2003008868	A1	20030109	US 2002-143322	20020510
US 6852717	B2	20050208		
PRIORITY APPLN. INFO.:			US 2001-291425P	P 20010516
			WO 2002-US14733	W 20020508

GI



I

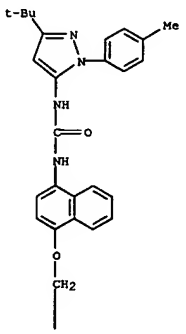
AB The title diaryl ureas, useful in pharmaceutic compns. for treating a cytokine mediated diseases or conditions involving inflammation such as chronic inflammatory diseases, were prepared Thus, treating 4-(2-chloropyrimidin-4-yloxy)naphthalen-1-ylamine with Et3N in DMF followed by addition of Et4NCN, and treatment of the resulting nitrile with phosgene, and reacting the intermediate with 5-tert-butyl-o-anisidine afforded the urea I.

IT 285983-44-0P 476010-09-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas as antiinflammatory agents)

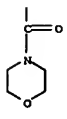
L7 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 285983-44-0 CAPLUS
CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



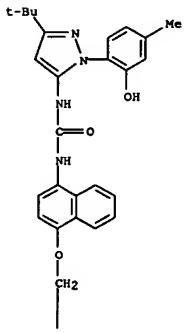
PAGE 2-A



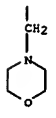
RN 476010-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(2-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 51 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

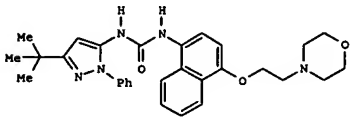


L7 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:658091 CAPLUS
DOCUMENT NUMBER: 137:185488
TITLE: Preparation of N-aryl-N'-azolylureas
INVENTOR(S): Tan, Zhulin; Song, Jinhua J.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066442	A1	20020829	WO 2002-US2982	20020101
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2435446	AA	20020829	CA 2002-2435446	20020101
EP 1362037	A1	20031119	EP 2002-707665	20020101
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004518739	T2	20040624	JP 2002-565959	20020101
US 2002123631	A1	20020905	US 2002-74895	20020212
US 6916924	B2	20050712		
PRIORITY APPLN. INFO.:			US 2001-268841P P	20010215
			WO 2002-US2982 W	20020101

OTHER SOURCE(S): CASREACT 137:185488; MARPAT 137:185488
GI



I

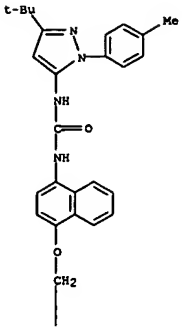
AB Title compds. were prepared Thus, 4-[2-(4-morpholinyl)ethoxy]-1-naphthaleneamine was N-acylated by ClCO2CH2CCl3 and the product amidated by 5-(1,1,-dimethylethyl)-1H-pyrazole-3-amine to give, after N-arylation, title compound I.

IT **285983-48-4P 451480-54-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of N-aryl-N'-azolylureas)

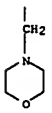
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



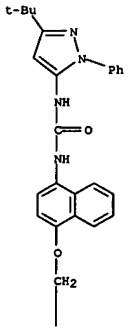
PAGE 2-A



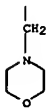
RN 451480-54-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 52 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:392357 CAPLUS
DOCUMENT NUMBER: 137:119059
TITLE: Pyrazole Urea-Based Inhibitors of p38 MAP Kinase: From Lead Compound to Clinical Candidate
AUTHOR(S): Regan, John; Breitfelder, Steffen; Cirillo, Pier; Gilmore, Thomas; Graham, Anne G.; Hickey, Eugene; Klaus, Bernhard; Madwed, Jeffrey; Moriak, Monica; Moss, Neil; Pargellis, Chris; Pav, Sue; Proto, Alfred; Swinamer, Alan; Tong, Liang; Torcellini, Carol
CORPORATE SOURCE: Research and Development Center, Department of Medicinal Chemistry, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(14), 2994-3008
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:119059

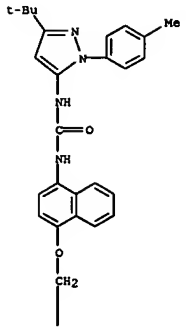
AB We report on a series of N-pyrazole, N'-aryl ureas and their mode of binding to p38 mitogen activated protein kinase. Importantly, a key binding domain that is distinct from the ATP (ATP) binding site is exposed when the conserved activation loop, consisting in part of Asp168-Phe169-Gly170, adopts a conformation permitting lipophilic and hydrogen bonding interactions between this class of inhibitors and the protein. We describe the correlation of the structure-activity relationships and crystallog. structures of these inhibitors with p38. In addition, we incorporated another binding pharmacophore that forms a hydrogen bond at the ATP binding site. This modification affords significant improvements in binding, cellular, and in vivo potencies resulting in the selection of Compound 45 (BIRB 796) as a clin. candidate for the treatment of inflammatory diseases.

IT **285983-48-4P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure activity relationships of N-pyrazole, N'-aryl ureas and their mode of binding to p38 mitogen activated protein kinase)

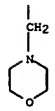
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 53 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



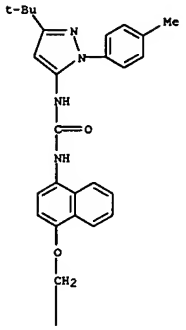
PAGE 2-A



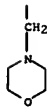
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L7 ANSWER 54 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:289124 CAPLUS
DOCUMENT NUMBER: 137:179568
TITLE: Anti-inflammatory effects of a p38 mitogen-activated protein kinase inhibitor during human endotoxemia
AUTHOR(S): Branger, Judith; Van den Blink, Bernt; Weijer, Sebastiaan; Madwed, Jeffrey; Bos, Carina L.; Gupta, Abhya; Yong, Chan-Loi; Polmar, Stephen H.; Olszyna, Dariusz P.; Hack, C. Erik; Van Deventer, Sander J. H.; Peppelenbosch, Maikel P.; Van der Poll, Tom
CORPORATE SOURCE: Laboratory of Experimental Internal Medicine and Department of Infectious Diseases, Tropical Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, 1105 AZ, Neth.
SOURCE: Journal of Immunology (2002), 168(8), 4070-4077
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The p38 mitogen-activated protein kinase (MAPK) participates in intracellular signaling cascades resulting in inflammatory responses. Therefore, inhibition of the p38 MAPK pathway may form the basis of a new strategy for treatment of inflammatory diseases. However, p38 MAPK activation during systemic inflammation in humans has not yet been shown, and its functional significance in vivo remains unclear. Hence, we exposed 24 healthy male subjects to an i.v. dose of LPS (4 ng/kg), preceded 3 h earlier by orally administered 600 or 50 mg BIRB 796 BS (an in vitro p38 MAPK inhibitor) or placebo. Both doses of BIRB 796 BS significantly inhibited LPS-induced p38 MAPK activation in the leukocyte fraction of the volunteers. Cytokine production (TNF-α, IL-6, IL-10, and IL-1R antagonist) was strongly inhibited by both low and high dose p38 MAPK inhibitor. In addition, p38 MAPK inhibition diminished leukocyte responses, including neutrophilia, release of elastase-α1-antitrypsin complexes, and up-regulation of CD11b with down-regulation of L-selectin. Finally, blocking p38 MAPK decreased C-reactive protein release. These data identify p38 MAPK as a principal mediator of the inflammatory response to LPS in humans. Furthermore, the anti-inflammatory potential of an oral p38 MAPK inhibitor in humans in vivo suggests that p38 MAPK inhibitors may provide a new therapeutic option in the treatment of inflammatory diseases.

IT 285983-48-4, BIRB 796 BS
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory effects of a p38 MAP kinase inhibitor BIRB 796 BS during human endotoxemia)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

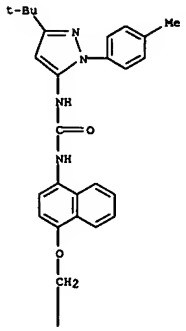
ACCESSION NUMBER: 2002:266137 CAPLUS
DOCUMENT NUMBER: 137:2372
TITLE: Inhibition of p38 MAP kinase by utilizing a novel allosteric binding site
AUTHOR(S): Pargellis, Christopher; Tong, Liang; Churchill, Laurie; Cirillo, Pier F.; Gilmore, Thomas; Graham, Anne G.; Grob, Peter M.; Hickey, Eugene R.; Moss, Neil; Pav, Susan; Regan, John
CORPORATE SOURCE: Department of Biology, Research and Development Center, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, 06877, USA
SOURCE: Nature Structural Biology (2002), 9(4), 268-272
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The p38 MAP kinase plays a crucial role in regulating the production of proinflammatory cytokines, such as tumor necrosis factor and interleukin-1. Blocking this kinase may offer an effective therapy for treating many inflammatory diseases. Here we report a new allosteric binding site for a diaryl urea class of highly potent and selective inhibitors against human p38 MAP kinase. The formation of this binding site requires a large conformational change not observed previously for any of the protein Ser/Thr kinases. This change is in the highly conserved Asp-Phe-Gly motif within the active site of the kinase. Solution studies demonstrate that this class of compds. has slow binding kinetics, consistent with the requirement for conformational change. Improving interactions in this allosteric pocket, as well as establishing binding interactions in the ATP pocket, enhanced the affinity of the inhibitors by 12,000-fold. One of the most potent compds. in this series, BIRB 796, has picomolar affinity for the kinase and low nanomolar inhibitory activity in cell culture.

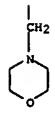
IT 285983-48-4, BIRB 796
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of p38 MAP kinase by utilizing novel allosteric binding site diaryl urea analog inhibitors for anti-inflammatory diseases)
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 55 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

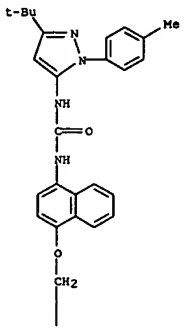
L7 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
returned to the drum to be mixed an addnl. 4 min under the same conditions. The resulting blend was then tabletted using tablet tooling and adjusting the tablet wt. for the appropriate potency. After the blend
was compressed into core tablets, the tablets were film coated. Tablets were coated to a wt. increase of 2-3%.

IT 285983-48-4, Birb 796
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral dosage formulations of (butyltolylpyrazolyl)-(morpholinylethoxy)naphthalenyl)urea)

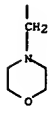
RN 285983-48-4 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L7 ANSWER 56 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:89870 CAPLUS
DOCUMENT NUMBER: 136:139863
TITLE: Improved oral dosage formulations of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]urea
INVENTOR(S): Cappola, Michael L.; Gereg, George W.; Way, Susan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007772	A2	20020131	WO 2001-US21860	20010711
WO 2002007772	A3	20021017		
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2415131	AA	20020131	CA 2001-2415131	20010711
US 2002031544	A1	20020314	US 2001-902822	20010711
US 6565880	B2	20030520		
EP 1305050	A2	20030502	EP 2001-984305	20010711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004504360	T2	20040212	JP 2002-513505	20010711
US 2003091636	A1	20030515	US 2002-282383	20021029
US 6808721	B2	20041026		
PRIORITY APPLN. INFO.:			US 2000-220387P	P 20000724
			US 2001-902822	A3 20010711
			WO 2001-US21860	W 20010711

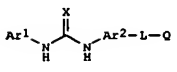
AB A process for preparing improved oral dosage forms of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-ylethoxy)naphthalen-1-yl]urea (Birb 796) (I) (I), with anti-inflammatory properties. Granulation of I within specified ranges provides improved dissoln. of the drug and oral bioavailability, as well as content uniformity. Incorporation into the formulation of an aqueous soluble inclusion compound capable of forming a complex
with I, such as β-cyclodextrin provides enhanced stability of the drug, in particular in highly ionic environments. Chipping and disintegration of tablets containing >10% β-cyclodextin can be prevented by applying a polymeric coat to the surface of the tablet at <40°. BIRB 796, lactose monohydrate, and povidone were dry mixed in a drum mixer
for 5 min. The resulting dry mix was then granulated in a shear mixer with water. The wet granules were then spread onto stainless steel trays and dried in an oven at 40-50° to an LOD of 2%. The dried granules were then milled through an 18-mesh screen in a cone mill. Microcryst. cellulose, pregelatinized starch, sodium starch glycolate, and colloidal silicon dioxide were then screened through an 18-mesh screen into the milled granules and the resulting mixture mixed in a drum mixer for 12 min
at approx. 30 rpm. Magnesium stearate, a lubricant, was then pre-blended with some of the mixed blend, screened through an 18 mesh screen and

L7 ANSWER 57 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN

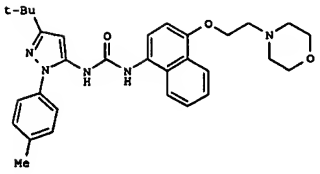
ACCESSION NUMBER: 2001:50642 CAPLUS
DOCUMENT NUMBER: 134:86264
TITLE: Novel process for synthesis of heteroaryl-substituted ureas
INVENTOR(S): Zhang, Lin-Hua; Zhu, Lei
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004115	A2	20010118	WO 2000-US17655	20000627
WO 2001004115	A3	20010927		
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2374737	AA	20010118	CA 2000-2374737	20000627
EP 1200411	A2	20020502	EP 2000-941745	20000627
EP 1200411	B1	20051214		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2003504366	T2	20030204	JP 2001-509725	20000627
AT 312823	E	20051215	AT 2000-941745	20000627
US 6583282	B1	20030624	US 2000-611109	20000706
US 2003109703	A1	20030612	US 2002-300448	20021120
US 6753426	B2	20040622		
US 2003166930	A1	20030904	US 2003-361719	20030210
US 6774233	B2	20040810		
US 2003166931	A1	20030904	US 2003-361731	20030210
US 6835832	B2	20041228		
US 2003181718	A1	20030925	US 2003-361440	20030210
US 6894173	B2	20050517		
PRIORITY APPLN. INFO.:			US 1999-143094P	P 19990709
			WO 2000-US17655	W 20000627
			US 2000-611109	A1 20000706

OTHER SOURCE(S): CASREACT 134:86264; MARPAT 134:86264
GI



I



II

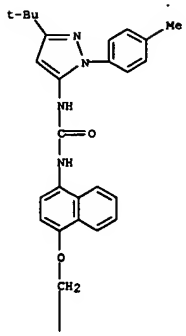
AB The title compds. [I; Ar1 = (un)substituted Ph, pyridinyl, pyrazolyl, etc.; Ar2 = (un)substituted Ph, naphthyl, quinolinyl, etc.; L = alkylene wherein one or more methylene groups are optionally replaced by O, N, or S, and substituted with 0-2 oxo groups and one or more alkyl, or L = cycloalkyl or cycloalkenyl optionally substituted with 1-2 oxo, 1-3 alkyl, alkoxy, alkylamino, etc., Q = (un)substituted Ph, naphthyl, pyridinyl, etc.; X = O, S], useful in pharmaceutic compns. for treating diseases or pathol. conditions involving inflammation such as chronic inflammatory diseases (no data), were prepared E.g., a multi-step synthesis of the urea II was given.

IT **285983-48-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(novel process for synthesis of heteroaryl-substituted ureas)

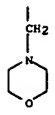
RN 285983-48-4 CAPLUS

CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

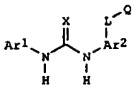


ACCESSION NUMBER: 2000:513688 CAPLUS
DOCUMENT NUMBER: 133:120325
TITLE: Preparation of aromatic heterocyclic ureas as antiinflammatory agents
INVENTOR(S): Cirillo, Pier F.; Gilmore, Thomas A.; Hickey, Eugene R.; Regan, John R.; Zhang, Lin-Hua
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

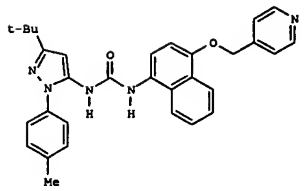
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043384	A1	20000727	WO 1999-US29165	19991209
W: AE, AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, VN, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2352524	AA	20000727	CA 1999-2352524	19991209
EP 1147104	A1	20011024	EP 1999-960668	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916930	A	20011030	BR 1999-16930	19991209
EE 200100376	A	20021015	EE 2001-376	19991209
EE 4527	B1	20050815		
JP 2003535023	T2	20031125	JP 2000-594800	19991209
RU 2220142	C2	20031227	RU 2001-122111	19991209
AU 770581	B2	20040226	AU 2000-17522	19991209
NZ 513525	A	20040528	NZ 1999-513525	19991209
TR 200102072	T2	20041221	TR 2001-200102072	19991209
TW 546297	B	20030811	TW 2000-89100638	20000117
US 6333325	B1	20011225	US 2001-871559	20010531
ZA 2001004656	A	20030210	ZA 2001-4656	20010607
US 6329415	B1	20011211	US 2001-891579	20010626
US 2002065285	A1	20020530	US 2001-891820	20010626
US 6506748	B2	20030114		
BG 105653	A	20020131	BG 2001-105653	20010627
HR 2001000516	A1	20020831	HR 2001-516	20010710
NO 2001003559	A	20010718	NO 2001-3559	20010718

PRIORITY APPLN. INFO.:
US 1999-116400P P 19990119
WO 1999-US29165 W 19991209
US 2000-484638 A1 20000118

OTHER SOURCE(S): MARPAT 133:120325
GI



I



II

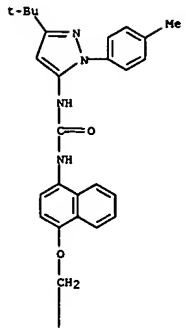
AB The title compds. [I; Ar1 = (un)substituted pyrrole, pyrrolidine, pyrazole, etc.; Ar2 = (un)substituted Ph, naphthyl, quinoline, etc.; L = (un)saturated (un)substituted carbon chain wherein one or more methylene groups are optionally replaced by O, N, or S; Q = (un)substituted Ph, naphthyl, pyridinyl, etc.], useful in pharmaceutic compns. for treating diseases or pathol. conditions involving inflammation such as chronic inflammatory diseases, were prepared E.g., a multi-step synthesis of the urea II was given. Representative compds. I were evaluated and showed IC50 of < 10 μM against TNF production in THP cells.

IT **285983-44-0P 285983-47-3P 285983-48-4P**
285983-49-5P 285983-51-9P 285983-54-2P
285983-56-4P 285983-57-5P 285983-58-6P
285983-64-4P 285983-68-8P 285983-74-6P
285983-87-1P 285983-89-3P 285983-90-6P
285983-92-8P 285983-95-1P 285983-96-2P
285983-97-3P 285983-98-4P 285983-99-5P
285984-00-1P 285984-01-2P 285984-02-3P
285984-03-4P 285984-04-5P 285984-06-7P
285984-07-8P 285984-08-9P 285984-09-0P
285984-10-3P 285984-11-4P 285984-12-5P
285984-13-6P 285984-20-5P 285984-21-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic heterocyclic ureas as antiinflammatory agents)

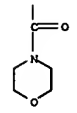
RN 285983-44-0 CAPLUS

CN Morpholine, 4-[[[4-[[[[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]amino]carbonyl]amino]-1-naphthalenyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

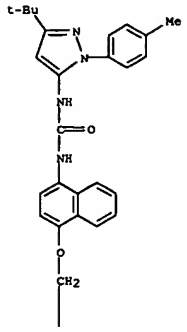


PAGE 2-A

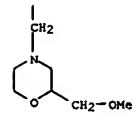


RN 285983-47-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[2-(methoxymethyl)-4-morpholinyl]ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

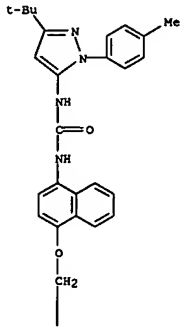


PAGE 2-A

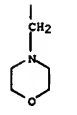


RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

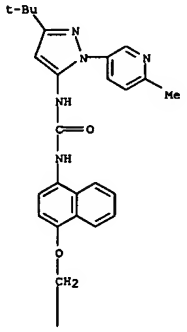


PAGE 2-A

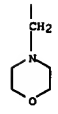


RN 285983-49-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

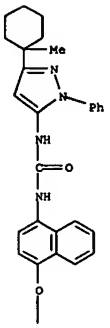


PAGE 2-A

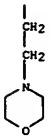


RN 285983-51-9 CAPLUS
CN Urea, N-[3-(1-methylcyclohexyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

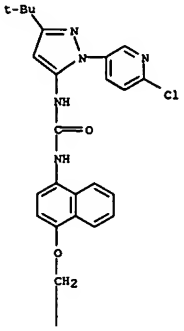


PAGE 2-A

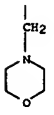


RN 285983-54-2 CAPLUS
CN Urea, N-[1-(6-chloro-3-pyridinyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

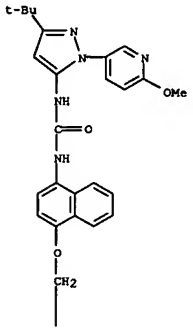


PAGE 2-A

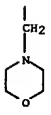


RN 285983-56-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methoxy-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

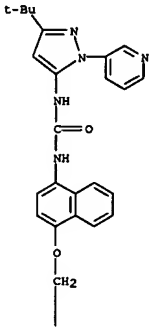


PAGE 2-A

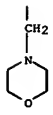


RN 285983-57-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

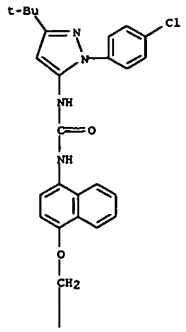


PAGE 2-A

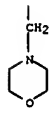


RN 285983-58-6 CAPLUS
CN Urea, N-[1-(4-chlorophenyl)-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

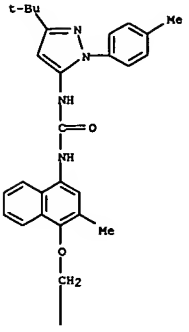


PAGE 2-A

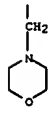


RN 285983-64-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[3-methyl-4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

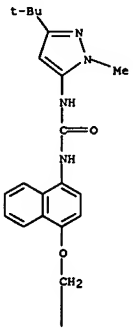


PAGE 2-A

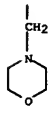


RN 285983-68-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

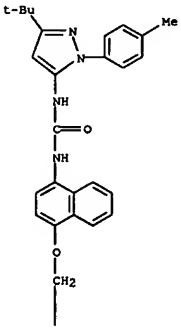


PAGE 2-A

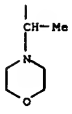


RN 285983-74-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)propoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

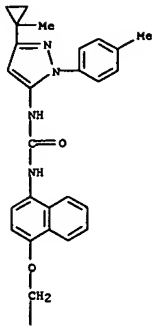


PAGE 2-A

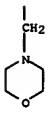


RN 285983-87-1 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



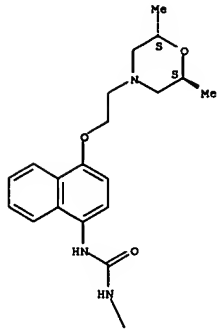
PAGE 2-A



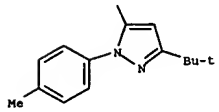
RN 285983-89-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



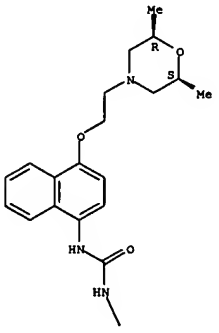
PAGE 2-A



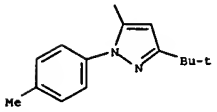
RN 285983-90-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A

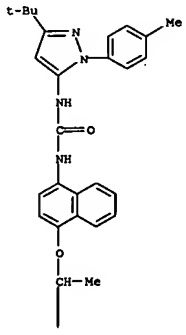


PAGE 2-A

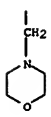


RN 285983-92-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[1-methyl-2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

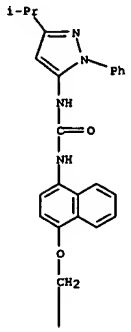


PAGE 2-A

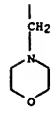


RN 285983-95-1 CAPLUS
CN Urea, N-[3-(1-methylethyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

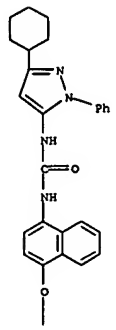


PAGE 2-A

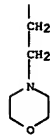


RN 285983-96-2 CAPLUS
CN Urea, N-(3-cyclohexyl-1-phenyl-1H-pyrazol-5-yl)-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

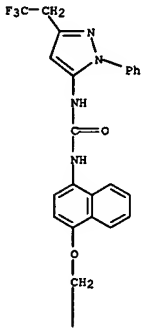


PAGE 2-A

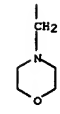


RN 285983-97-3 CAPLUS
CN Urea, N-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-N'-[1-phenyl-3-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

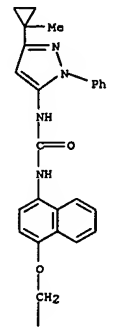


PAGE 2-A

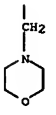


RN 285983-98-4 CAPLUS
CN Urea, N-[3-(1-methylcyclopropyl)-1-phenyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

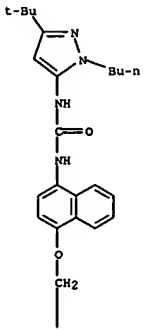


PAGE 2-A

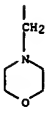


RN 285983-99-5 CAPLUS
CN Urea, N-[1-butyl-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

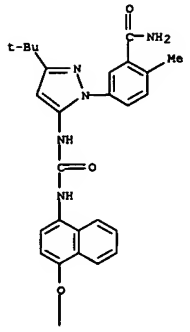


PAGE 2-A

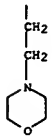


RN 285984-00-1 CAPLUS
CN Benzamide, 5-[3-(1,1-dimethylethyl)-5-[[[[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]amino]carbonyl]amino]-1H-pyrazol-1-yl]-2-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

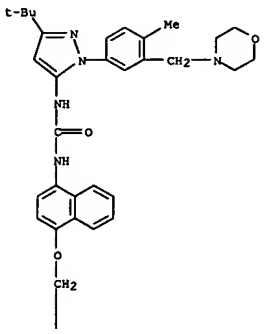


PAGE 2-A

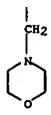


RN 285984-01-2 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-methyl-3-(4-morpholinylmethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

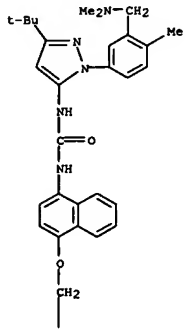


PAGE 2-A

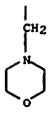


RN 285984-02-3 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]-4-methylphenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



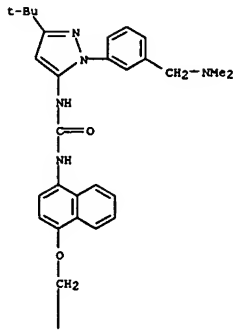
PAGE 2-A



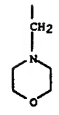
RN 285984-03-4 CAPLUS
CN Urea, N-[1-[3-[(dimethylamino)methyl]phenyl]-3-(1,1-dimethylethyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

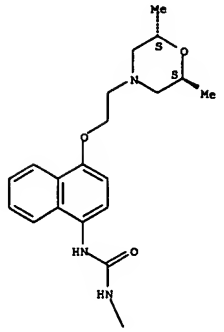


RN 285984-04-5 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-[(2R,6R)-2,6-dimethyl-4-morpholinyl]ethoxy]-1-naphthalenyl]-, rel- (9CI) (CA INDEX NAME)

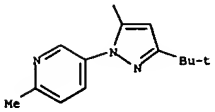
Relative stereochemistry.

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



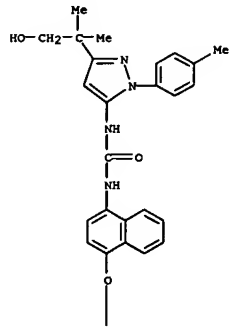
PAGE 2-A



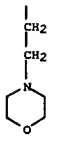
RN 285984-06-7 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



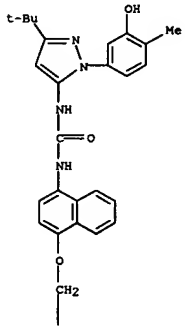
PAGE 2-A



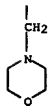
RN 285984-07-8 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(3-hydroxy-4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

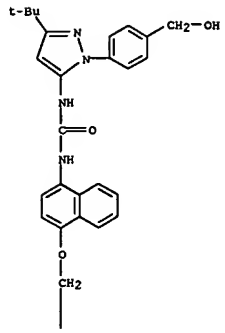


PAGE 2-A

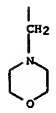


RN 285984-08-9 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-[4-(hydroxymethyl)phenyl]-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

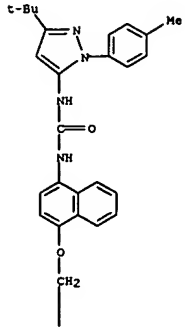


PAGE 2-A

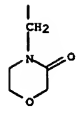


RN 285984-09-0 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(3-oxo-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

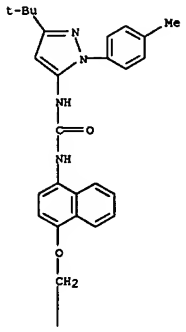


PAGE 2-A

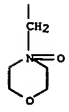


RN 285984-10-3 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

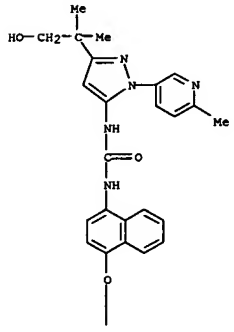


PAGE 2-A

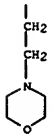


RN 285984-11-4 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



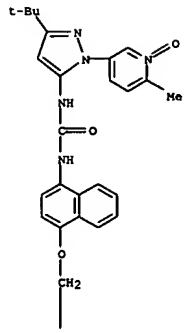
PAGE 2-A



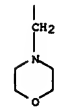
RN 285984-12-5 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-(6-methyl-1-oxido-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



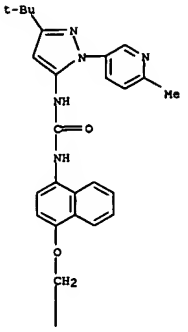
PAGE 2-A



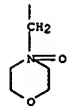
RN 285984-13-6 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(6-methyl-3-pyridinyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



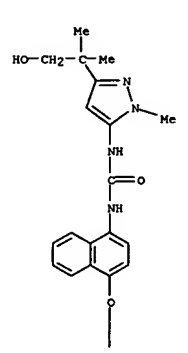
PAGE 2-A



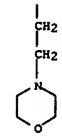
RN 285984-20-5 CAPLUS
CN Urea, N-[3-(2-hydroxy-1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



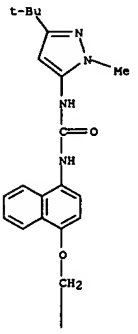
PAGE 2-A



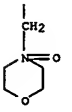
RN 285984-21-6 CAPLUS
CN Urea,
N-[3-(1,1-dimethylethyl)-1-methyl-1H-pyrazol-5-yl]-N'-[4-[2-(4-oxido-4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 58 OF 58 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

```
=> d his

     (FILE 'HOME' ENTERED AT 11:47:10 ON 27 MAY 2006)

     FILE 'REGISTRY' ENTERED AT 11:47:17 ON 27 MAY 2006
L1             STRUCTURE UPLOADED
L2               8 S L1
L3              98 S L1 FULL
L4              98 S L3 AND CAPLUS/LC

     FILE 'CAPLUS' ENTERED AT 11:47:42 ON 27 MAY 2006
L5              61 S L3
L6               3 S L3 AND ETHANOL
L7              58 S L5 NOT L6

=> s l7 and diffraction
        424723 DIFFRACTION
          1444 DIFFRACTIONS
        425366 DIFFRACTION
                  (DIFFRACTION OR DIFFRACTIONS)
L8              1 L7 AND DIFFRACTION

=> s l7 and x-ray
       1513592 X
       1021288 RAY
        217942 RAYS
       1099619 RAY
                  (RAY OR RAYS)
        809649 X-RAY
                  (X(W)RAY)
L9              3 L7 AND X-RAY
```

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:547258 CAPLUS
DOCUMENT NUMBER: 143:65486
TITLE: Polymorphs of BIRB 796 and their preparation
INVENTOR(S): Smoliga, John A.; Vitous, Jana
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005137195	A1	20050623	US 2004-10975	20041213
WO 2005063715	A1	20050714	WO 2004-US41627	20041213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-530834P P 20031218

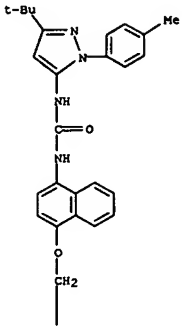
AB Disclosed are polymorphs of 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)-naphthalen-1-yl]-urea and processes from making the same. A polymorph form VI of BIRB 796 possessing a solid-solid polymorphic transformation in the range of 138 -145° to Form VII which subsequently melts in the range of 177-186°. A process of preparing a BIRB 796 polymorph form VI process comprises: dissolving BIRB 796 in a solvent chosen from Et acetate, Bu acetate, iso-Bu acetate, iso-Pr acetate, Pr acetate and tert-Bu acetate at reflux temperature; cooling the solution to about room temperature and subsequently collecting the crystallizing solid. XRPD data of polymorph form VI of BIRB 796 are listed.

IT **285983-48-4**, BIRB 796
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polymorphs of BIRB 796 and their preparation)

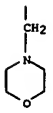
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1072170 CAPLUS
DOCUMENT NUMBER: 142:190226
TITLE: Interaction Profiles of Protein Kinase-Inhibitor Complexes and Their Application to Virtual Screening
AUTHOR(S): Chuaqui, Claudio; Deng, Zhan; Singh, Juswinder
CORPORATE SOURCE: Computational Drug Design Group, Department of Research Informatics, Biogen Idec, Inc., Cambridge, MA, 01242, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(1), 121-133
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

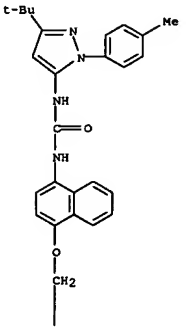
AB A major challenge facing structure-based drug discovery efforts is how to leverage the massive amount of exptl. (x-ray and NMR) and virtual structural information generated from drug discovery projects. Many important drug targets have large nos. of protein-inhibitor complexes, necessitating tools to compare and contrast their similarities and differences. This information would be valuable for understanding potency and selectivity of inhibitors and could be used to define target constraints to assist virtual screening. The authors describe a profile-based approach that enables us to capture the conservation of interactions between a set of protein-ligand receptor complexes. The use of profiles provides a sensitive means to compare multiple inhibitors binding to a drug target. The authors demonstrate the utility of profile-based anal. of small mol. complexes from the protein-kinase family to identify similarities and differences in binding of ATP, p38, and CDK2 compds. to kinases and how these profiles can be applied to differentiate the selectivity of these inhibitors. Importantly, our virtual screening results demonstrate superior enrichment of kinase inhibitors using profile-based methods relative to traditional scoring functions. Interaction-based anal. should provide a valuable tool for understanding inhibitor binding to other important drug targets.

IT **285983-48-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(interaction profiles of protein kinase-inhibitor complexes and their application to virtual screening)

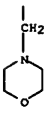
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:839017 CAPLUS
DOCUMENT NUMBER: 142:311699
TITLE: Structural insights into the conformational selectivity of STI-571 and related kinase inhibitors
AUTHOR(S): Mol, Clifford D.; Fabbro, Doriano; Hosfield, David J.
CORPORATE SOURCE: Syrrx Inc, La Jolla, CA, 92121, USA
SOURCE: Current Opinion in Drug Discovery & Development (2004), 7(5), 639-648
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

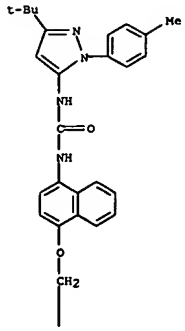
AB A review. STI-571 (Gleevec) is a highly successful cancer drug due to its activity as an inhibitor of the Abelson cytoplasmic tyrosine kinase (Abl), which is constitutively active in a majority of patients with chronic myelogenous leukemia. STI-571 also inhibits two type III receptor tyrosine kinases, c-Kit and platelet-derived growth factor receptor, and functions by targeting inactive conformations of these kinases. This review focuses on recent developments in x-ray co-crystal structure analyses of STI-571 bound to Abl and the c-Kit receptor tyrosine kinase domain, and also three other relevant kinase inhibitor co-crystal structures. The similar structural features of these inactive kinases suggest they will be useful for the successful drug discovery and development of specific and targeted gene-based cancer drugs.

IT 285983-48-4, BIRB-796
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural insights into the conformational selectivity of STI-571 and related kinase inhibitors)

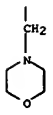
RN 285983-48-4 CAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	338.17	510.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-48.00	-48.00

STN INTERNATIONAL LOGOFF AT 11:49:35 ON 27 MAY 2006